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OF
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THIRD SERIES FOUNDED BY EDWARD JACKSON

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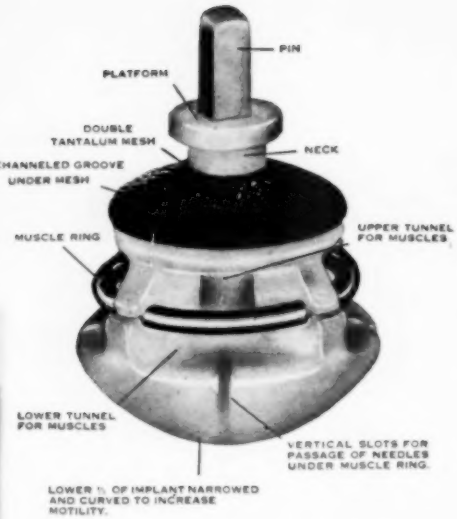

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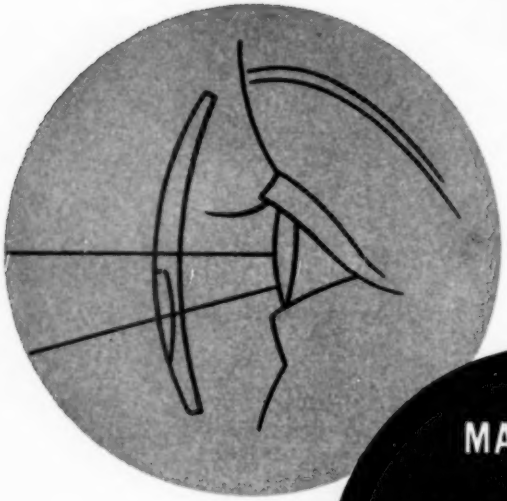

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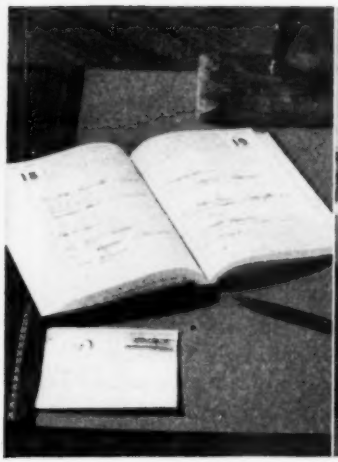

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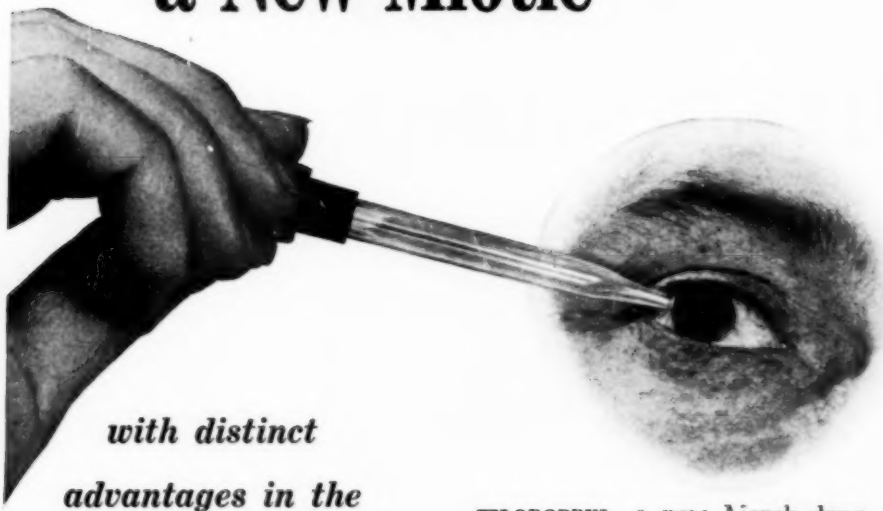

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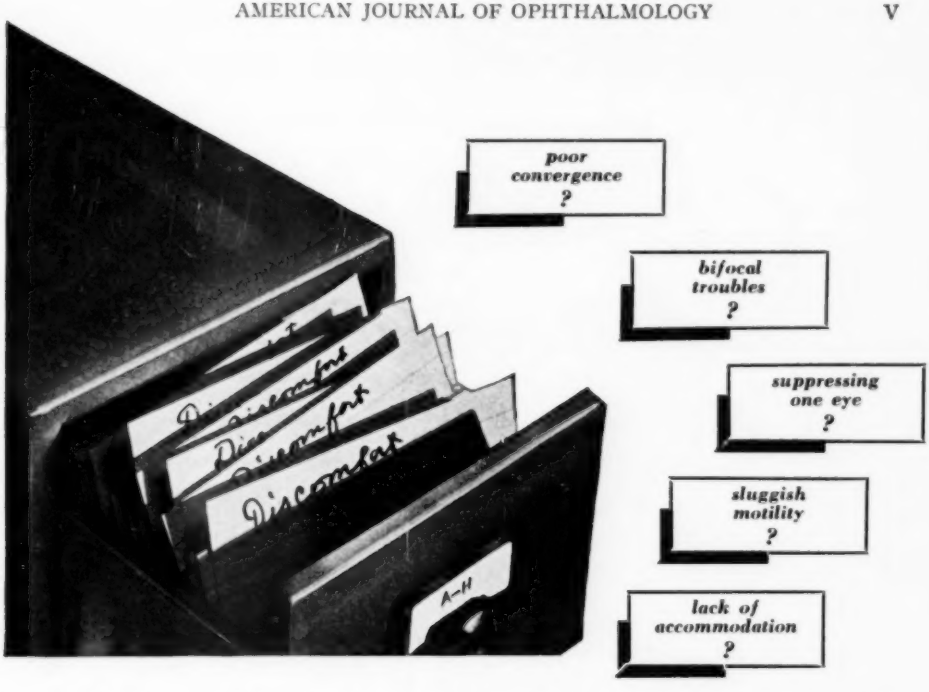

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TABLE #1 READING DISTANCES

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+2.00	11 INCHES	20 INCHES
+2.50	12 INCHES	17 INCHES
+3.00	12 INCHES	14 INCHES

Table 1, above gives the approximate reading range that can be expected through the various reading additions. It is also important, when ordering trifocals, to know how much greater range can be expected through the intermediate segment.

Table 2 gives the approximate range through the intermediate portions of the trifocals. It should be understood that both Table 1 and Table 2 give approximations and not exact distances. The accommodation is such a variable factor that only approximations are possible. However, the distances given in the tables are correct enough for most cases.

TABLE #2 INTERMEDIATE DISTANCE

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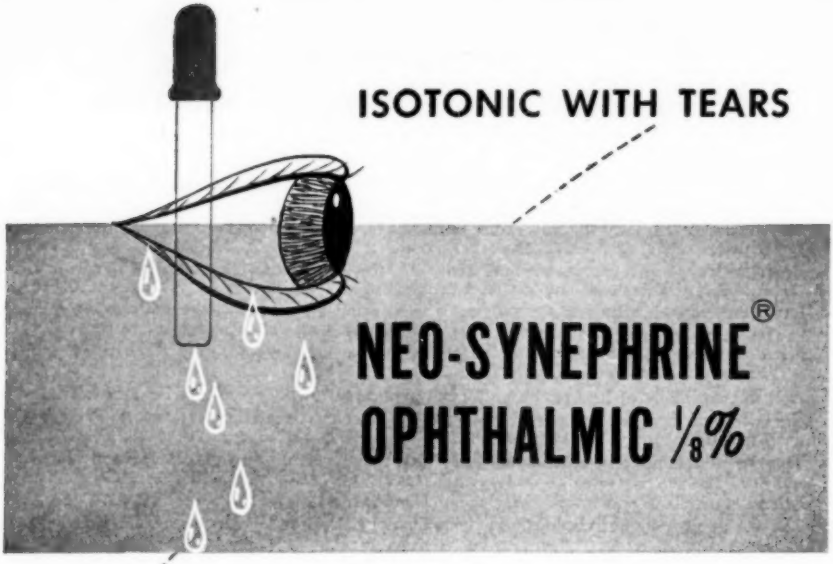

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FIG. 1 (CORDES AND HOGAN). FUNDUS PHOTOGRAPH, SHOWING THE LESION AND THE FINGERLIKE PROJECTIONS INTO THE SURROUNDING RETINA.

AMERICAN JOURNAL OF OPHTHALMOLOGY

VOLUME 32 AUGUST, 1949 NUMBER 8

PRIMARY MALIGNANT MELANOMA OF THE OPTIC DISC*

REPORT OF A CASE

FREDERICK C. CORDES, M.D., AND MICHAEL J. HOGAN,† M.D.
San Francisco, California

Primary tumors of the optic disc are among the more rare neoplasms encountered in ophthalmology. Of the various types seen, the primary malignant melanoma is the most unusual. According to the literature this uncommon condition has been confirmed microscopically only five times.

Other types are less rare and among those reported have been angio-endothelioma,[1] fibroma,[2] endothelioma,[3] perithelioma,[4] and peripapillary melanosarcoma.[5] Rönne[6] states that most of the tumors of the optic disc are malignant, although Kurzezunge and Pollack[7] and Carruthers[8] observed cases for some time without any evidence of growth.

OPTIC-NERVE TUMORS

Optic-nerve tumors are seen also in tuberous sclerosis. According to Reese,[9] characteristically they are single or multiple, whitish to yellowish tumors, which vary a great deal in size and may reach an elevation of five diopters or more. Usually they have a nodular or mulberrylike surface and have been described as appearing like a localized accumulation of frog eggs or tapioca grains. These mulberrylike tumors on the disc have been reported by van der Hoeve,[10] Messinger and Clark,[11] Reese,[9] Nitsch,[12] and others.

In angiomatosis retinae (Hippel-Lindau disease), the angioma may take the form of a localized, sharply defined, raspberrylike tumor of the disc as reported by Niccol and Moore.[13] The eye was removed after the patient consulted another ophthalmologist "who came to the conclusion that the risk of malignancy could not be excluded." One of us observed a similar case at Dibble General Hospital during World War II, in which the histologic diagnosis was made by the Army Medical Museum.

Davis,[14] in this monumental work on primary tumors of the optic nerve associated with von Recklinghausen's disease, found 32 authentic cases showing this relationship. Among cases of this type was one reported by Stallard[15] on the occurrence of a tumor of the left optic disc in a youth, aged 19 years, whose left eye was removed for a supposed malignant neoplasm. Later, symptoms of a brain tumor developed, and the patient died after an exploratory operation. From the family history and the data at hand, Stallard felt that there could be little doubt that the lesion of the disc was part of a neurofibromatosis with involvement of the optic and auditory nerves as well as the brain.

Van der Hoeve[16] expressed the belief that tuberous sclerosis, multiple neurofibromatosis (von Recklinghausen's disease), Hippel-Lindau disease, and the Sturge-Weber syndrome are all related and have the same underlying pathologic process. He suggested

* From the Division of Ophthalmology, University of California Medical School. This work was made possible by funds from the Mr. and Mrs. Berthold Guggenhime Donation. Presented at the 84th annual meeting of the American Ophthalmological Society, Hot Springs, Virginia, May, 1948.

† By invitation.

calling the entire group the "phakomatoses" (phakos, "mother spot").

Drusen of the optic disc

Drusen of the optic disc may at times suggest a tumor. In a case reported by Reese[9] there was an elevation of four diopters. In a case reported by Samuels[17] the formation lay under a heavily pigmented covering. Lauber[18] also reported an elevated disc as the result of extensive drusen formation. Reese[9] feels that drusen of the optic nerve are a feature of the congenital developmental anomaly known as tuberous sclerosis. Wagener[19] is of the opinion that drusen of the optic nerve are really slow-growing asteróblastomas of hereditary and familial occurrence.

Cysts may resemble tumors at times. Both congenital and acquired cysts of the papilla have been reported by Verhoeff,[20] Hilgartner,[21] Levine,[22] Rothmund,[23] and others, and may be congenital, follow tuberous sclerosis, or result from a cystic degeneration of a tumor as in one of Verhoeff's cases, where a cyst was found on the disc in a case of glioma of the optic nerve.

Gummata of the optic disc are rather rare but, as Parsons[24] states, they may simulate an intraocular tumor. In the case reported by Scheidemann,[25] the gumma of the disc had this appearance, ophthalmoscopically. Juler[26] reported a similar case that microscopically showed a diffuse leukocytic infiltration of the nerve, retina, and choroid.

Malignant melanoma

In the literature, seven cases have been cited as being examples of primary malignant melanoma of the optic disc. The first to be reported (in a short 2-page account) was that of Murray[27] in 1910. In his patient, a 66-year-old man, the papilla "was completely obscured by a pearly gray spheroid body, apparently the diameter of the disc and pedunculated. Had appearance of cyst attached apparently to the center of the disc."

The complete microscopic examination given is as follows: "The tumor lies between the sclera and retina. The portion of the retina lies stretched over the tumor. The tumor is considerably thinned out and disorganized so that its characteristic anatomic structure is lost.

"The tumor cells do not extend into the sclera at all. There is considerable diffuse infiltration of tumor cells in the loose connective tissue lying in the angle between the retina and the sclera at the point where they separate to cover the tumor."

The diagnosis made was small spindle-cell sarcoma. No mention is made of the choroid and there is no indication in the illustrations, which are drawings, as to whether or not the choroid was involved. From the above, it is apparent that this case cannot be included among the "proved" examples of primary malignant melanomas of the disc.

In 1911, Vasquez-Barrière[28] reported a tumor of the optic nerve in a 32-year-old man. The tumor was heavily pigmented and measured 3½ by 5¾ mm.; it was hourglass-shaped and involved both the optic nerve and papilla. Microscopic examination revealed a heavily pigmented small round-cell sarcoma of the optic nerve with some secondary involvement of the adjacent choroid. Fry and De Long[29] felt that this tumor was probably a malignant melanoma that originated in the choroid near the optic-nerve entrance and involved the optic nerve secondarily. Vasquez-Barrière had considered this possibility and concluded that it could be ruled out. He stated that Axenfeld, after having examined the serial sections, was also of the opinion that the tumor was primary in the nervehead. This case has been generally accepted as being primary on the disc.

In 1915, Oloff[30] reported what clinically appeared to be a primary malignant melanoma of the optic disc in a 22-year-old sailor. Following enucleation, the eye was cut sagittally and a macroscopic diagnosis made of sarcoma of the optic disc that did not extend

beyond the lamina cribrosa. There was some pigment present. Microscopic study was impossible because the specimen was lost during the confusion associated with the mobilization of Germany for World War I. This report, therefore, cannot be included in the cases of proved primary malignant melanoma of the optic disc.

In 1923, Cosmettatos[31] described a primary malignant melanoma of the papilla in a 40-year-old man. Ophthalmoscopically, the disc was elevated and there were some retinal hemorrhages along the vessels. Microscopic examination revealed that the tumor involved the intraocular portion of the optic nerve as well as the nerve behind the lamina cribrosa. There was no choroidal involvement. Reese[35] felt that this case could be considered a primary melanosarcoma of the papilla which arose in the region of the lamina cribrosa.

In 1925, Speciale-Cirincione[32] described a primary pigmented sarcomatous tumor of the optic nerve occurring in a 32-year-old man. The mass which covered the papilla extended into the vitreous. Microscopic examination revealed a conical, elevated mass extending from the disc into the vitreous for 4 mm. On one side, the mass extended a short distance into the choroid where the tumor was pigmented. The mass was considered to be a sarcomatous tumor which arose in the papilla and invaded the near-by choroid secondarily. Fry and De Long[29] felt that this tumor in all probability was also a malignant melanoma, primary in the choroid. Speciale-Cirincione was of the opinion that, due to the fact that the largest portion of the tumor was on the papilla and was without pigment, the tumor could be considered as being primary in the papilla, and that if the neoplasm had arisen in the choroid, pigment would not have been lacking. Reese[35] also considered this tumor as being primary in the optic disc.

Oguchi[33] reported a malignant melanoma of the disc in a 21-year-old man. In the left eye, the entire disc was covered by a heavily pigmented mass that extended into the vitreous for 4 to 5 diopters. Microscopically the tumor, a malignant melanoma of the mixed-cell type, involved the entire disc and extended a short distance into the nerve trunk. "Aside from the disc and the optic nerve, no other changes were found in the entire globe." Oguchi, in his summary, states that ophthalmoscopically the tumor was on the disc and microscopically showed no involvement of the choroid, so that there can be no doubt that this tumor was primary in the optic disc.

Levine,[34] in 1935, reported a primary melanosarcoma of the disc in a 53-year-old Puerto Rican. Ophthalmoscopically, the right disc showed a protrusion of the upper temporal portion of the optic disc into the vitreous for a distance of three diopters. Microscopic examination revealed a densely pigmented mass which occupied almost the entire upper half of the disc and extended with the latter into the interior of the eye for 2 mm. Some pigment-laden cells were present in the rod and cone and outer and inner nuclear layers, but the remainder of the retina was entirely normal. The tumor evidently originated in the upper temporal part of the disc in front of the lamina cribrosa and grew forward and somewhat nasally, pushing the papilla into the vitreous humor and bending the columns of nerve fibers and their supporting tissue nasally. The choroid was entirely spared in all the sections studied and even where the tumor mass entirely surrounded it, the choroid was not invaded by tumor cells. The tumor extended along the optic nerve beyond the point of cutting the optic nerve. There can be little doubt that this tumor did not originate in the choroid.

Case report

Mrs. Viola E. S., a Negress, aged 52 years (O.P.D. No. 134309), was first seen in the Eye Clinic on December 5, 1946, having been referred from the Hypertension Clinic for Keith-Wagener classification of vascular changes.

History. There were no specific complaints regarding the eyes except slight blurring of vision of

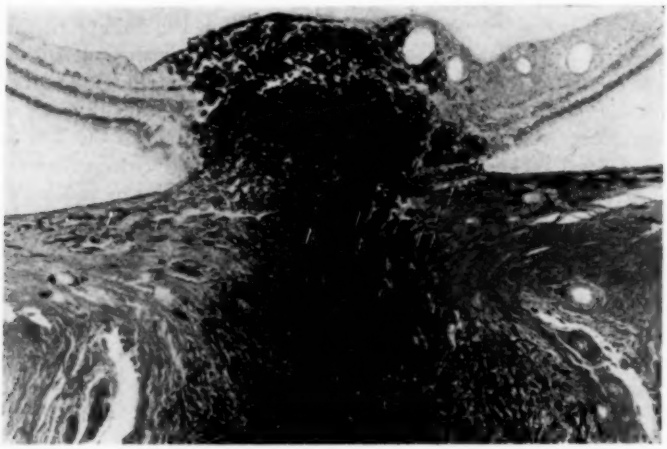

Fig. 2 (Cordes and Hogan). Section through the tumor.

the right eye. Past history was unimportant.

Eye examination. Vision was: R.E., 20/30; with correction, 20/20. L.E., 20/20; with correction, 20/20. *Right eye:* External examination negative. Fundus: Negative except for moderate vascular changes (Keith-Wagener II). *Left eye:* External examination negative. Fundus: Media clear. Disc: The inferior portion of the disc was covered by a dark, pigmented, slightly elevated, circumscribed mass approximately one disc diameter in size. The inferior temporal vessels crossed over the mass. The remainder of the fundus was normal except for the above-mentioned vascular changes.

Perimetric field studies revealed on the screen a superior enlargement of the blindspot.

Intraocular pressure was well within normal limits.

Physical examination. The physical examination was irrelevant. A search failed to reveal any evidence of metastatic lesions or primary malignancy elsewhere in the body.

Laboratory tests were negative except for a positive test to coccidioidin, 1:100.

A fundus photograph was not obtained because the retinal camera was being overhauled at this time.

The patient returned on March 6, 1947, at which

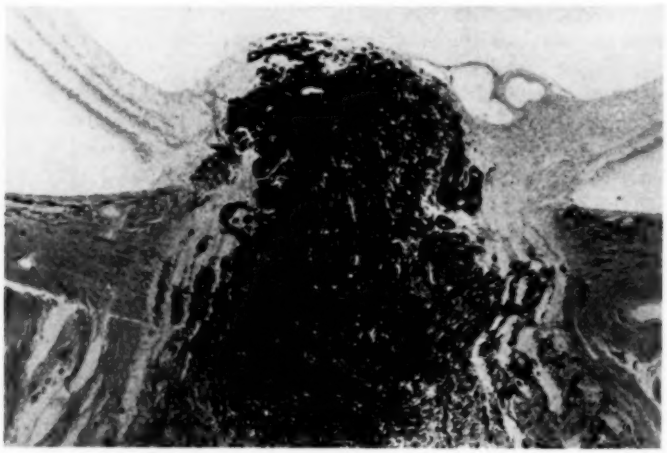

Fig. 3 (Cordes and Hogan). Section through the tumor.

time a fundus photograph was taken. Examination revealed a noticeable extension of the tumor mass with fingerlike projections into the surrounding retina. The tumor appeared blacker and more elevated and the inferior temporal vessels were covered (fig. 1).

A diagnosis of malignant melanoma of the optic disc was made; enucleation of the left eye was advised and performed.

Report of Eye Pathology

Gross examination. The specimen is a left eye which measures 26 by 25 by 25 mm. The optic nerve measures 10 mm. Transillumination is normal. Vertical calottes were made. The vitreous appears normal and the retina is in situ. The lens is clear and in its normal position. There is a black tumor on the optic disc which extends very slightly into the lower retina. The tumor appears to occupy the lower one third of the disc and does not extend laterally to the subretinal or retinal tissues. On sectioning the nerve, the tumor appears to extend beyond the lamina cribrosa, but not beyond the point of excision of the eye. No extension through the posterior scleral emissaria is noted.

Microscopic examination. The entire globe is normal except for the disc and retina.

Choroid. The choroid is thin and flat and rather heavily pigmented throughout. Serial sections were made of the eye, extending from one margin of the disc to the other. There is no evidence that the tumor of the disc arose from choroidal tissues and extended into the optic nerve. In several areas, there are very thin strands of tumor which extend toward the border tissue but do not appear continuous with the choroidal stroma.

Optic nerve. The disc is the site of a very darkly pigmented tumor, seeming to arise mainly from the tissues of the nerve anterior to the lamina cribrosa. This tumor extends laterally in the nerve into tissues surrounding the nerve. Anteriorly, the cells extend into the retina a short distance along the vessels. Posteriorly, the tumor extends about 3 mm. beyond the outer scleral opening of the optic nerve canal (figs. 2, 3, and 4).

Sections were depigmented and the cells were found to be fairly large and slightly pleomorphic. Most of them are round or spindle-shaped, with moderate cytoplasm which accepts a pale stain. The nuclei are oval or rounded and the nuclear chromatin shows clumping and is abundant. Almost all of the cells contain one or more nucleoli. Occasional hyperchromatic nuclei are seen. There are no true mitoses (figs. 5 and 6).

Diagnosis. Malignant melanoma, optic disc.

Fig. 4 (Cordes and Hogan). Section through the tumor. This and Figures 2 and 3 are part of serial sections, showing that there was no involvement of the choroid.

Comments

Of the 7 reported cases of primary malignant melanoma of the optic disc, only 5 can be considered as "proved" cases; namely those of Vasquez-Barrière, Cosmettatos, Speciale-Cirincione, Oguchi, and Levine.

Murray's case may have been another, but the incomplete description and the statement that " the tumor lies between the sclera and retina" prevents acceptance of this case. Oloff's report is based entirely on the oph-

thalmoscopic picture and on a macroscopic diagnosis of a cut made sagittally through the enucleated eye and, while the clinical and

Fig. 5 (Cordes and Hogan). Depigmented section through the tumor.

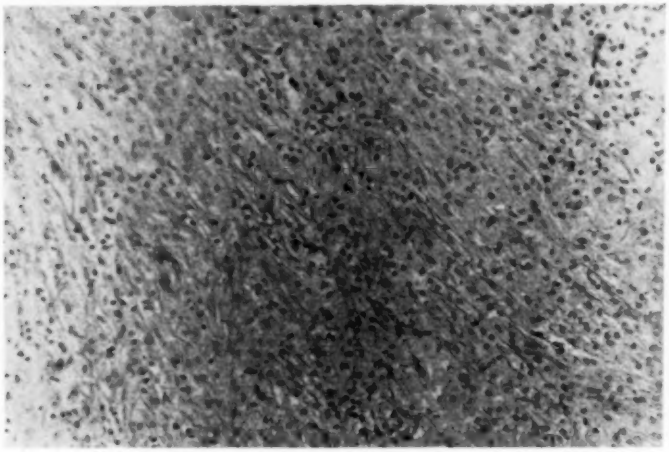

Fig. 6 (Cordes and Hogan). A low-power view through the depigmented section of the tumor.

macroscopic findings seem to justify the diagnosis, it cannot be included in the "proved" cases.

In only 3 of these cases (Cosmettatos, Oguchi, Levine) was there no involvement of the choroid. While there has been some question of Vasquez-Barrière's report because of the choroidal involvement, the evidence in favor of its being an extension from the primary tumor is strong enough to warrant its acceptance. In Speciale-Cirincione's case, while there is involvement of the choroid, the evidence presented seems

to warrant the contention that it can be considered a primary tumor of the optic disc.

In our case, serial sections through the tumor revealed only a few very thin strands of tumor tissue which extended into the border tissue at its junction with the choroid but which did not appear continuous with the choroidal mesoderm. We therefore feel that this case can be added to those that have been considered "proved" cases of primary malignant melanomas of the optic disc.

Site of origin

As Reese[35] has pointed out, cases of malignant melanoma of the disc reported from clinical appearance without microscopic substantiation must be regarded with some doubt, since the far more common juxtapapillary malignant melanoma of the choroid may appear to arise from the disc. Reese, in his paper, illustrates this point by sections from such a case. In these cases, the growth begins in the choroid adjacent to the disc, proceeds along the course of least resistance around the termination of the lamina vitrea, through the intermediary tissue of Kuhnt, and lobulates over the internal surface of the optic nervehead. Since the major portion of the tumor and its farthest extension into the vitreous is over the disc, is appears clinically to arise from the disc.

The case reported by Fry and De Long[29] clinically suggested a tumor primary in the disc. After microscopic study they concluded that the point of origin of the tumor probably was from choroidal elements at the lower inner margin of the disc or misplaced choroidal elements within the disc itself.

Verhoeff[36] also felt that this tumor rose at the side of the disc. Similar cases where the tumor clinically appeared to arise from the disc but revealed upon examination that it really had its origin in the choroid have been reported by Prevec,[37] Bucalessi,[38] and others.

A like case was seen by Dr. Owen Dickson of the university staff who was good enough to permit us to examine the patient. Ophthalmoscopically, the tumor measured about two disc diameters in size with one third of the tumor on the disc. It was elevated four diopters. Microscopically, it was apparent that the tumor, a malignant melanoma, arose from the choroid at the inferior edge of the disc.

In considering primary tumors of the optic disc, it is to be remembered that in addition to arising from the choroid, the tumors may have their origin in the optic nerve behind the lamina cribrosa. Stallard[15] reported a hemispherical mass of newly formed tissue projecting from the disc in a young man, aged 19 years; this proved to be a neuroma of the optic nerve associated with von Recklinghausen's disease. Salzer[39] found the greatest part of a sarcoma which was visible on the disc to be located in the optic nerve itself.

Samuels[40] in discussing Fry and De Long's paper, pointed out that in any tumor of the eye, including those of the disc, one must keep in mind that the first clinical manifestations of a tumor elsewhere in the body may be found in the fundus of an eye. Davis[41] reported a metastatic carcinoma of the breast. Heine[42] reported a metastatic melanosarcoma of the disc and Schiess-Gemuseus and Roth[43] reported a sarcoma of the disc that was also metastatic.

Cordes and Horner[44] reported a case of metastases to the optic nerve as well as other structures occurring one year after removal of a congenital nevus of the left scapula. The nevus had developed a troublesome itching which the patient tried to relieve by scratching. This was followed by active growth of the nevus.

Brömser[45] reported metastasis to the eye one year after removal of a rapidly growing pigmented nevus of the cheek. Schiess-Gemuseus and Roth's[43] patient developed a metastatic melanosarcoma of the choroid one year after the removal of a growing congenital pigmented nevus over the sternum.

Pflüger's[46] patient developed a similar condition one year after the removal of a congenital nevus over the parotid region following growth resulting from scratching to relieve extreme itching.

Thus, there are four cases in which metastases appeared one year after the removal of a growing congenital pigmented nevus. It is interesting that in Levine's case, reported under primary malignant melanomas of the disc, there is a history of removal of a pigmented mole of the right thigh because of persistent itching, one year before the appearance of the tumor of the disc. Six months after the enucleation, the patient reported "that his health was excellent." It would be interesting to know whether or not there was any relationship between the nevus and the tumor of the disc.

Source of pigment

The source of pigment is of interest in these primary malignant melanomas of the disc. In discussing pigmentation of the lamina cribrosa, Reese[35] states the the external laminae, or laminae scleralis, are continuations of the scleral elements adjacent to the nerve, while the internal laminae, or laminae choroidalis, are continuations of the choroidal elements by way of the border tissue. The lamina cribrosa, then, may be considered as potentially pigment-bearing tissue in which pigment may manifest itself in excessively pigmented persons or races.

He also observed that, adjacent to a temporal conus, the pigmented epithelium may extend a short distance into the disc. This may be an actual migration of the pigment into the periphery of the disc. It may be an extension of the pigmented epithelium into the nerve margin along with the lamina vitrea when the latter sometimes does not terminate at the nerve margin but extends a short distance into it. The small, isolated, clearly demarcated dots of pigment occasionally found in the nerve-fiber layer of the disc probably originate from the adjacent pigmented epithelium.

As Levine[34] has pointed out, areas of pigmentation about the disc and in the nerve proper are not uncommon and it is likely that benigh melanomas may be situated in the optic nerve. Ogawa[47, 48] emphasized the frequency of pigmentation of the optic nerve in the Japanese, as did also Oguchi.[33] In addition, it is generally recognized that this condition is fairly common in the Latin race.

Reese,[35] Scheerer,[49] and others have remarked on the frequency of the occurrence of pigmented cells in the optic nerve. Coats[50] was of the opinion that isolated pigment spots on the disc were due to a pigmentation of the lamina cribrosa. In discussing pigmentation of the optic disc, Juler and Mann[51] describe three types: (1) Dense isolated plaques which occupy a sector of the disc and extend into the surrounding retina (these vary from black to brownish gray, depending upon their location); (2) linear markings, commonly found on the temporal side near the disc edge, and curved concentrically with it; and (3) lacelike pigmented veins closely associated with the blood vessels.

Rönne[52] stated that isolated pigment spots on the disc have no practical significance. At times the pigmentation may be greater, so that the disc may be partially or entirely pigmented. For example, in the case reported by Pálish-Szántó[53] the temporal half of the disc was pigmented, while in the cases presented by Moehle[54] and Hirschberg[55] the entire disc was pigmented. Hirschberg's patient a child, aged 9 years, also showed excessive pigmentation of the iris and had a microcornea.

Sources of primary pigmented tumors

Of interest are the possible sources of the primary pigmented tumors of the optic nerve.

The various possible sources for these pigmented tumors found in and around the eye are discussed at length by Reese[56] in

his de Schweinitz Lecture on pigmented tumors. Cells which produce pigment are called melanoblasts and the pigment they produce is called melanin, a term applied to almost any black, brown, or tan pigment. There are two types of pigment encountered in the eye: that found in the pigment epithelium of the retina, which is black and composed of discrete rods, and the pigment found in the chromoblasts of the uvea, which is light and appears as amorphous, crystalline granules of varying sizes.

Bloch[57] has established the fact that melanoblasts contain an oxidase which is specific for oxidizing "dopa" (dihydroxyphenyl alanine) into a substance resembling melanin. According to Laidlaw[58] this oxidase is increased wherever melanin is being produced and is the invariable precursor of melanin. The oxidase appears in the cell some time before the resultant melanin is visible, and the melanin itself may remain in the cell long after the oxidase has disappeared.

According to Reese,[56] excess of oxidase is essential for a cell to fabricate melanin and when this oxidase is available many of the cells have the potentiality to show melanin in their protoplasm. The process of oxidation is responsible for the appearance of melanin in the protoplasm of a melanoblast. This seems to convert a preëxisting premelanin or melanogenic substance in the protoplasm into black or visible melanin.

Reese has divided melanoblasts from which tumors may arise into three types: (1) Neurogenic melanoblast, which includes the Schwann cell, the nevus cell, and the melanoblasts stemming from the secondary optic vesicle, the latter including the pigment epithelium of the retina; (2) ectodermal melanoblasts located in the basal layer of the skin and mucous membrane; and (3) the mesodermal melanoblasts found in the uvea and the sacral and extrasacral mongol spots.

In discussing the tumors arising from the pigment epithelium of the retina, Reese[56] states that these cells proliferate on the slightest provocation. When sufficiently provoked by pathologic processes, their hyperplasia may manifest itself in large plaques of tissue having the characteristics either of the mother epithelial cell or of the metaplastic fibrous tissue. Pure hyperplasia of these cells into tumorlike masses provoked by some chronic pathologic process within the eye produces the lesion usually seen, but in extremely rare instances a neoplasm, may arise from this hyperplasia. As has been noted already, pigmentation of the disc often is derived from the retinal pigment epithelium, so that it might be possible for a primary malignant melanoma of the disc to arise from these neurogenic melanoblasts.

As Reese further points out, the mesodermal melanoblasts are usually long, narrow, branching cells but when their pigment content is increased they take on a more polygonal or plump shape with few or no processes. Between these two extremes, there are transitional stages depending somewhat on the pigment content. These cells are found primarily throughout the uveal tract. They are usually referred to as chromatophores, which implies that they are pigment-harboring cells. He feels this is incorrect and that the cell is a true melanoblast and, therefore, should be referred to as a chromatoblast.

It is generally accepted that the uvea is mesodermal and therefore contains large numbers of melanoblasts which are mesodermal. Reese feels it is highly improbable that all the melanomas of the uveal tract are neurogenic or ectodermal in origin but that there is also a chromatogenic melanoma. The cell type is the mesodermal chromatoblast, which gives rise to tumors in the form of benign or malignant chromatogenic melanomas. The cell comprising these tumors has, for the most part, the characteristics of the chromoblast normally seen in the uvea. As pointed out by Reese,[25] Levine,[24] and others, the choroidal chromatoblasts (chromato-

phores) grow into the optic nerve with the lamina cribrosa as it spreads into the nerve. It is from these cells that the primary malignant melanomas may also possibly arise.

Thus malignant changes may occur in pigment cells on, or in, the disc which are derived from the retinal pigment epithelium (neurogenic melanoblasts), or from the chromatoblasts present in the lamina cribrosa (mesodermal melanoblasts).

Summary

A case of a primary malignant melanoma of the left optic disc in a 52-year-old Negress is presented. The growth appeared to arise from the tissues of the optic nerve anterior to the lamina cribrosa. There was some extension into the retina below, while the choroid showed no evidence of involvement.

There are two possible sources for the formation of these malignant melanomas of the disc. They may arise from the pigment cells in the nerve that are derived from the retinal pigment (neurogenic melanoblasts) or from the chromoblasts (mesodermal melanoblasts) that grew into the optic nerve with the lamina cribrosa.

The available literature reveals only five cases of primary malignant melanomas of the optic disc that can be considered proved cases. We feel justified in adding this report as the sixth case.

384 Post Street (8).

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THE TREATMENT OF LOCAL LID INFECTIONS WITH PHAGES AND PARTICULARLY WITH FILTRATES*

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With the introduction of the sulfa drugs and penicillin, the older forms of treatment for infections were practically swept out. Unfortunately, the use of sulfonamides and penicillin, locally, frequently results in severe dermatoses and allergic reactions. In addition, penicillin may so sensitize an individual that, when its use becomes essential, a severe and dangerous reaction may follow. Certainly, infections of the lids are rarely serious enough to warrant the parenteral introduction of these drugs. For the treatment of local infections, antibiotics were used long before the sulfa compounds and penicillin. However, reports of their use in this country are few.

My first acquaintance with the antibiotics was in 1928. After an incision and drainage for acute dacryocystitis, healing was extremely slow. The prolonged treatment and continuous purulent discharge was wearing on both patient and doctor. Irrigation of the wound with Bacteriophage (Parke Davis) and dressings wet with the overflow solution dried the wound in a few days and healing followed shortly. I have used Bacteriophage several times since then with excellent results.

REPORTS IN LITERATURE

Bacteriophage was first described by Pfeiffer[1] (1910 and 1912) but his work was not immediately reviewed in the English literature. Twort,[2] a few years later, independently described a curious degenerative change in a culture of staphylococcus. He was able to reproduce the condition by putting a drop of the highly diluted filtrate from the first culture into another culture of staphylococcus. However, it was d'Herelle[3] who really popularized the use of bacterial filtrates and who studied the phenomena most intensively.

In 1916, d'Herelle recorded a series of observations on the lytic properties of filtrates of mixed cultures obtained from the feces of patients suffering from bacillary dysentery.

* Presented before the New York Society for Clinical Ophthalmology, February 7, 1949.

D'Herelle called the lytic agent bacteriophage and believed it to be a filterable virus parasite which acted upon the bacterial cells. These phages are characterized by being able to pass through filters and also by acting on susceptible bacteria so as to bring about lysis during the phase of active bacterial growth. Phages act on specific bacteria and their related species.

D'Herelle's theory is virtually accepted at the present time, and recently Cohen[4] was able to synthesize these viruses from filtrates of B. coli and to study their protein makeup.

In 1924, Besredka[5] observed that when pure cultures of bacteria were grown in broth for 2 or 3 weeks, and the cultures filtered through Berkefeld candles, the filtrates inhibited the growth of the original organism. The topical application of these filtrates also produced a local immunity against the organisms used in the preparation of the filtrate. The action was not lytic, as with bacteriophage, but bacteriostatic and immunizing. Besredka called these soluble antigens, antivirus. Grossman[6] called them auto-antibiotics.

Although phages and filtrates are both prepared by filtering bacterial cultures and seem to be related in their therapeutic activity, they are not the same. Phage is an autolytic agent, probably a bacterial virus, and is heat labile. Antivirus is bacteriostatic, not lytic, and is heat stable.

The excellent therapeutics results of these bacterial filtrates, separated from the phages, have been confirmed by a great number of clinical reports, principally in Europe. Besredka has summarized many of these reports and discussed their use in corneal infections, dacryocystitis, conjunctivitis, blepharitis, and so forth.

In this country, there have been only two recent publications on the use of bacterial filtrates, one by Grossman[6] on their use in infections of the external ear and nose, and the other by Combes[7] on the treatment of skin infections. Combes's contribution included two cases of blepharitis, this being the only reference to the use of filtrates in ophthalmology. It would seem, therefore, that a report on the clinical use of bacterial filtrates in 116 cases of lid infections is in order.

Clinical use

In this series, the youngest patient treated was aged 2 years, the oldest 67. Antipeol ointment* was used because of the excellent results obtained in a few cases treated with samples sent by the company.

The ointment is prepared according to the method of Besredka from bacterial filtrates of Staphylococcus aureus, albus, and citreous; Streptococcus viridans, pyogenes, and hemolyticus; and B. pyocyaneus. These filtrates are mixed in a lanolin base containing sulfo-icthyolate, sodium borate, and zinc oxide. Some criticisms and suggestions on the composition of the ointment base will be mentioned later.

Of the 116 cases, 70 were single infected chalazions. The infections cleared up entirely in 66 cases; in 51 so completely that no trace of the chalazions remained. In 15 cases, the infection subsided so that within a few days the chalazions were excised. In only 1 of 8 cases of multiple infected chalazions was the course of infection not influenced favorably. The others cleared completely and, in 2 cases, surgical removal of the chalazions followed.

Antipeol ointment was used in 4 cases of single and 7 cases of multiple hordeola. In all cases, the infections cleared promptly, usually in 1 or 2 days. There were 2 cases of chalazions with blepharitis; neither was improved. In 12 cases of blepharitis, 1 was greatly improved and 1 moderately improved; 8 were not improved; while, in 2 cases, the lid conditions were made worse. Of 3 cases of lid abscess, 2 were cured within 3 days and 1 was not improved so that incision was necessary.

* Produced by the Bio-Therapeutic Laboratories, Inc. East Orange, New Jersey.

Antipeol was very effective in 6 cases of acute dacryocystitis. In none of these were incision and drainage necessary. Three cases of pericanalicular infection (lower puncta) responded promptly and quickly to treatment. There was one case of serious infection of a lid following a burn. Healing was quick and with a minimal formation of scar tissue.

Case reports

Case 1. J. S., a man, aged 67 years, had a large infected chalazion of the right upper lid, so large as to simulate a lid abscess. In two days, all signs of inflammation subsided and, in a short while, the process had absorbed so that no traces of the chalazion remained.

Case 2. I. F., a man, aged 42 years, had an infected chalazion of the left upper lid for which another ophthalmologist had prescribed penicillin salve. He developed a severe local reaction, although the chalazion was in no way influenced. The skin reaction and infection subsided promptly with Antipeol.

Case 3. S. M., a woman, aged 56 years, had been a severe diabetic for many years. She had an infected chalazion in the left upper lid. Four days later, the infection and chalazion had disappeared.

Case 4. A. M., a boy, aged 5 years, had multiple infected chalazions of the right upper lid. In a few days, the infection and chalazions had disappeared.

Case 5. A. R. a boy, aged 7½ years, had multiple recurrent hordeola and, for over a year, had never been without several of them. These disappeared following several applications of the ointment. He was subsequently treated with an autogenous vaccine and has had no recurrences in over 3 years.

Case 6. H. L., a girl, aged 6 years, had a chronic blepharitis of several years' duration. Treatment with Antipeol over a period of several months cured the condition. Whenever the lids showed any signs of irritation, she used the ointment for a few days. Her lids have remained in a very satisfactory condition for over 3 years.

Case 7. A. B., a young woman, aged 24 years, had a chronic blepharitis of several years' duration. She had received a variety of treatments by a number of ophthalmologists. With the use of Antipeol there was immediate improvement but, in a short time, the blepharitis returned and was not influenced further.

Case 8. I. D., a man, aged 50 years, had a chronic blepharitis of many years' duration. Some hot, soapy solution, used to clean milk bottles, had splashed into his eyes and, shortly after, he had developed a severe ulcerative blepharitis which resisted many forms of treatment, including Antipeol. The condition responded rapidly to penicillin.

Case 9. J. A. S., a girl, aged 2 years, had an acute dacryocystitis on the right side for 3 days. The acute condition subsided completely with 2 applications of Antipeol.

Case 10. E. K., a woman, aged 34 years, had an acute dacryocystitis on the left side for which sulfa powders had been prescribed by another ophthalmologist. She had taken 20 powders without any effort. The infection subsided with 2 applications of Antipeol. Removal of the sac was advised but this the patient refused because of a bad cardiac condition. Her heart barely compensated under normal conditions. Two months later, the dacryocystitis recurred but subsided promptly with Antipeol. Again, removal was refused. Several months later, while I was away, the acute condition recurred. Another ophthalmologist incised the sac. Several weeks later, the sac was removed.

Case 11. E. C., a woman aged 42 years, had an acute dacryocystitis on the left side which responded rapidly to Antipeol. Although the sac was not removed, there has been no recurrence in over 2 years.

Case 12. L. R., a woman, aged 55 years, had an acute dacryocystitis on the left side about 7 months prior to her visit. The condition never completely subsided but "flared up" every week or two. About a week before her visit, she developed an acute episode which showed no tendency to subside. In fact, the pain was quite unbearable. A few applications of Antipeol resulted in a rapid and prompt subsidence of the infection. The sac was removed 2 months later.

Case 13. A. J., a woman, aged 60 years, had an acute dacryocystitis on the right side which subsided rapidly with Antipeol treatment. The sac was removed several weeks later.

Case 14. G. C., a woman, aged 68 years, had an acute dacryocystitis of the right side. The condition responded promptly to 2 applications of Antipeol.

Case 15. H. P., a man, aged 33 years, had an abscess of the left upper lid of unknown origin. The abscess was completely resolved after 4 applications of Antipeol.

Case 16. N. T., a man, aged 22 years, had a cellulitis of the right lower lid following a respiratory infection. Antipeol did not affect the lid infection.

Case 17. G. F., a woman, aged 43 years, had an abscess of the right upper lid which followed plucking of the eyebrow. The infection subsided promptly with Antipeol.

Case 18. M. L. M., a woman, aged 45 years, had an infection around the canaliculus of the left lower lid. Cure was prompt with Antipeol.

Case 19. S. C., a man, aged 36 years, had a pericanalicular infection of the right lower lid. Healing followed one application of Antipeol.

Case 20. M. F., a man, aged 62 years, had a pericanalicular infection of the right lower lid which disappeared following one application of Antipeol.

Case 21. F. M., a man, aged 25 years, was stir-

ring hot chocolate when some of the contents splashed in his face. The left upper lid became infected. The infection subsided rapidly with Antipeol treatment. Healing was excellent and with a minimal formation of scar tissue.

Discussion

One of the criticisms of the product (Antipeol) is that the ointment is too thick and difficult to remove. The greatest complaint made by the patients was that they could not get the ointment out from between the lashes without considerable rubbing. Possibly this aggravated the blepharitis which might otherwise have shown better response. If the filtrate could be incorporated in an ointment which had the consistency of the average ophthalmic ointment, this might be obviated. In addition, a softer ointment might permit better diffusion of the filtrate, with better results. At this time, a thought occurs that a filtrate of pyocyaneous germs in a suitable base might become an important adjunct in the treatment of pyocyaneous ulcers of the cornea so common in industrial injuries.

Conclusion

While it is true that a great many local infections of the lids are self-limited and get well with the simple use of hot compresses, the rapid and excellent results in the 116 unselected cases reported and in a number of cases treated since are definite proof of the beneficial effects of bacterial filtrates on the ordinary pyogenic infections.

The results were more gratifying because of the complete absence of local allergic reactions. An unusual and striking phenomenon was the rapid relief from pain.

Some suggestions on the improvement of the product are offered. Wider treatment with bacterial phages and filtrates is recommended to avoid unnecessary allergic reactions and complications from the use of penicillin and sulfa drugs, which can always be used if the phages and filtrates fail.

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Ophthalmic Miniature

There is only one kind of chalazion. Its cause is the collection of a gross humor that gathers in the lid. It occurs most frequently in the outer aspect of the lid, and appears as a hard swelling, just like a hailstone.

Treatment. Dissolve gum ammoniac or galbanum in strong vinegar and rub it on the tumor; or one may apply a salve of roses mixed with wax and turpentine.

Memorandum Book of a Tenth-Century Oculist
Translated by Casey A. Wood.

REGENERATION OF THE CORNEAL STROMAL CELLS*

II. Review of literature and histologic study

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In the course of studies on the fate of corneal grafts[1, 2] a clear understanding of the mode of regeneration of the corneal stromal cells was found to be essential in order to determine whether the cells in the donor cornea were replaced or not. A technique[3] was devised whereby the corneal cells could be destroyed with minimal inflammatory reaction and minimal disturbance of the corneal lamellae. It is the purpose of this report to describe the histologic appearance of these lesions and to establish the source of the regenerated stromal cells.

Review of the literature

Regeneration of the corneal stromal cells has been studied extensively in the past. The types of injury used to produce destruction of these cells have been penetrating and nonpenetrating incisions into the anterior and posterior surface of the cornea and chemical burns of the cornea. Cell replacement in some cases of parenchymatous keratitis has also been studied.

It has been concluded from these observations that the stromal cells are replaced from: (1) Undamaged corneal corpuscles; (2) wandering cells from outside of the cornea; (3) a transformation of epithelial cells or endothelial cells into stromal cells; and (4) a combination of these sources.

Most workers have based their conclusions on the morphologic appearance of the cells in the regenerating area. The methods used in studying the regeneration of the stromal cells and the conclusions drawn from these studies are so similar in many instances that a detailed review of each report will not be given.

Gueterbock, Gussenbauer, Reich, Neelson and Angelucci, and others[4a–d] made incisions of various types into the cornea of frogs, rabbits, and dogs and concluded from their studies that the destroyed stromal cells were replaced from undamaged corneal corpuscles in the region of the lesions. They noted that mitotic figures appeared in the cells adjacent to the injury and that the cells became more spindle in shape before migrating into the injured area. The possibility that these newly formed cells could have originated from cells outside of the cornea was thought to have been eliminated by the scarcity of wandering cells observed in the undamaged part of the cornea.

The same conclusions were reached by Eberth,[5] Senftleben,[6] Homen,[7] and Klemensiewicz,[8] following studies on lesions produced by chemical injuries of the cornea. Elschnig[9] and Fuchs[10] studied the regeneration of stromal cells in human eyes which had been injured by inflammatory processes and had been removed for various reasons. They were not as dogmatic in their opinions as to the origin of the newly formed stromal cells but they also thought that the majority of the cells originated from undamaged corneal corpuscles. Fuchs observed the scarcity of cells containing mitotic figures and suggested that the stromal cells in some cases divided by amitosis.

Ranvier[11] offered the unique theory that wounds in the cornea were repaired by protoplasmic outgrowths from the stromal cells and not by a multiplication of these cells. Kruse,[12] who worked in Grawitz's laboratory, thought that the newly formed stromal cells arose from the "slumbering cells" of Grawitz.[13] He studied many tissues of the body and concluded that specific cells existed in the various connective tissues which could not be seen in normal tissue

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with hematoxylin and eosin stain. If, however, the tissue was injured these cells became activated to repair the lesion and could be seen with routine stain. Neither of these theories has been confirmed.

Retterer[14] studied incisions in guinea pigs' corneas and concluded that the new stromal cells originated from transformed epithelial cells and a multiplication of the stromal cells by mitotic division.

Salzer[15a–e] made extensive studies on incisions performed from the external surface in the cornea of rabbits, guinea pigs, frogs, trout, chickens, pigeons, and salamanders. In a series of articles, he gradually came to the conclusion that the epithelial cells, which migrate into a wound made from the external surface of the cornea, are converted into stromal cells. As proof of this he stated that he was able to follow the transition from a typical epithelial cell to a spindle cell of the stroma.

He also thought that the nuclei of the newly formed corneal corpuscles showed a remarkable similarity to the nuclei of the epithelial cells. The protoplasma of the newly formed spindle cells (keratoblasts) stained with hematoxylin like the protoplasma of the epithelial cells.

Salzer was unable to find stromal cells in the process of multiplication and offered this as evidence against the participation of stromal cells in repair.

Wolfrum and Boehmig[16a–b] disputed the epithelial origin of stromal cells. They concluded from a series of experiments in which incisions were made into the posterior surface of the cornea that the stromal cells were replaced by mitotic and amitotic division of the corneal corpuscles and in some instances by a transformation of the endothelial cells. They thought that the leukocytes played no part in the regeneration of the stromal cells.

Hanke[17] studied perforating and nonperforating wounds in guinea pigs' corneas. He thought that the newly formed corneal corpuscles were derived from the undamaged stromal cells and, in some instances, from the endothelial cells in the deeper layers of perforating wounds. In order to determine whether or not macrophages participated in the repair of corneal stromal cells he tagged these cells by injecting trypan blue into the animals, systemically. A few cells containing this dye were found in the area of active repair. Hanke thought that these cells were not derived from outside of the cornea for he could not find cells containing the dye in the normal cornea between the lesions and limbus.

Von Wyss,[18] Bonnefont and Lacoste,[19] and Janyk,[20] on the other hand, have suggested that destroyed corneal cells are replaced by leukocytes or macrophages which wander into the cornea after injury. They thought that the stromal cells did not aid in this reparative process.

Pullinger and Mann[21] have recently studied rabbits injected with pontamine sky blue in which the corneal cells had been destroyed by applying a small droplet of liquid mustard gas to the center of the cornea. They were unable to follow the complete transition of macrophages containing this dye to stromal cells because the dye tended to disappear just at the time when the cells changed their characteristics.

However, they concluded from their experiments that most probably the principal source of newly formed corneal corpuscles was the conversion of macrophages. They pointed out that, embryologically, the corneal corpuscles were derived from wandering mesodermal cells which phagocytize vital dyes. They also stated that, in only a few instances, were corneal corpuscles observed in the process of division and therefore it was unlikely that these cells participated very actively in the process of repair.

Scelkunow[22] reported that regenerated stromal cells were derived from corneal corpuscles and leukocytes.

It may be concluded from this review of

the literature that newly formed stromal cells are derived from several sources but that there is no uniformity of opinion as to the source of these regenerated cells. The proof offered in most instances as to the origin of these cells has been based on routine histologic examinations. In only a few instances have special techniques been used to establish the source of the cells. Because of this diversity of opinion and the lack of substantial proof of any one theory it was thought that the source of the regenerating stromal cells should be investigated further.

Experimental studies

The corneal cells in rabbits and rats were destroyed by freezing the tissue to −78°C. for 3 to 5 seconds according to the technique previously described.[3] In rabbits' corneas, 2-mm. and 6-mm. lesions produced a slight edema of the cornea which could be seen grossly 2 to 3 hours after freezing. This edema increased up to 24 hours, persisted for a few days, and gradually absorbed leaving the corneas entirely normal in appearance on gross and slitlamp examinations 5 to 7 days after freezing.

The persistence of the edema was proportional to the duration and area of freezing. Central corneal lesions on the whole caused less reaction in the conjunctiva and iris than peripheral injuries. Vascularization of the cornea was never observed in central injuries and only rarely were a few small capillaries noted to invade the cornea for a few millimeters after peripheral lesions. Secondary infection occurred in only a few instances in which over half of the corneal cells were destroyed at one time and there was persistent edema of the cornea.

Rats' corneas reacted in a similar manner but they normally contain more polymorphonuclear cells and tend to develop more inflammatory reaction. The advantage of studying rats' corneas is that the epithelium can be removed and a central 2- to 3-mm. strip consisting of the whole thickness of the stroma can be stained and examined under a microscope without sectioning. This allows a greater number of stromal cells to be observed at one time.

Histologic study

This study is based on 158 eyes removed at 5 minutes, 15 minutes, 30 minutes, 1 hour, every hour up to 4 hours, at a 3-hour interval up to 24 hours, every day up to 13 days, every other day up to 20 days, and then every 4 days up to 48 days.

Five minutes after the application of a 6-mm. solid brass applicator (cooled to −78°C.) to the cornea of a rabbit for three seconds the epithelium in the area of injury is missing. This loss of epithelium may be due to the adherence of the epithelium to the applicator.

Within 15 minutes after injury the endothelial cells in the region of freezing become flatter than normal and a few of the cells are detached from Descemet's membrane. Fibrinous exudate appears in the anterior chamber. In 30 minutes, edema can be seen in the posterior layers of the stroma. Two hours after injury a marked loss of endothelium can be observed and a few polymorphonuclear cells appear in the anterior chamber.

At this time the first changes are seen in the stromal cells. The corneal corpuscles in the area which has been frozen become thinner than normal and take a more basophilic stain. The stromal cells just adjacent to the injury become swollen. The edema which was present only in the posterior layers of the cornea can now be seen throughout the full thickness of the tissue. The corneal lamellae are separated by edema but otherwise appear normal.

At 4 hours after injury definite fragmentation of the nuclei of the endothelial cells (fig. 1) can be observed and more of these cells have become detached from the endothelium. The "stringlike" appearance of the stromal cells is more obvious. The edema

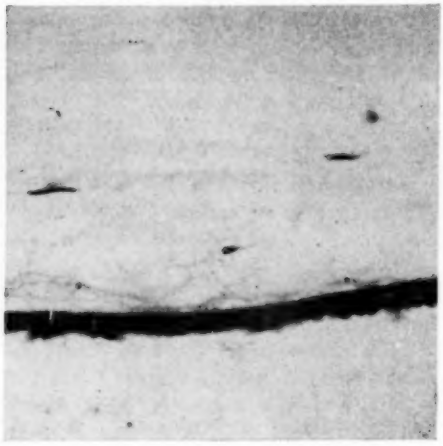

Fig. 1 (Maumenee and Kornblueth). Central freezing of rabbit's cornea (6 mm./3 sec.) four hours after injury, showing nuclear fragmentation of endothelial cells and stringlike stromal cells. (Hematoxylin-eosin stain. ×500.)

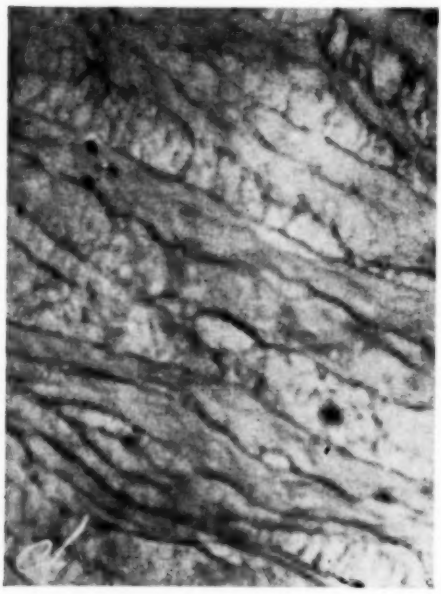

Fig. 2 (Maumenee and Kornblueth). Central freezing of rabbit's cornea (6 mm./3 sec.) 10 hours after injury, showing nuclear fragmentation of stromal cells. (Hematoxylin-eosin stain. ×500.)

of the stroma increases and a few polymorphonuclear cells can be seen outside of the vessels in the conjunctiva.

By 6 hours the endothelium is completely lost in the region of the injury. Fragmentation of the nuclei can be observed in the stromal cells and many of these cells have disappeared from the lesion.

At 10 hours most of the stromal cells have disappeared and those that remain show fragmentation of the nuclei (fig. 2). A few polymorphonuclear cells can be seen under the epithelium in the region of injury for the first time. The polymorphonuclear cells have increased in number at the limbus but the reaction is still not great. At 12 hours the cornea in the area which was frozen is practically acellular (figs. 3 and 4). The corneal edema has increased so that the thickness is now about three times greater than normal.

Very little further change is noted in the cornea until about 20 to 24 hours after freezing when definite signs of repair appear. Possible slight migration of the epithelium and endothelium occurs before this time but now regeneration of these tissues becomes definite.

The cells in the basal layers of the epithelium become flattened and at times spindle-shaped. They migrate in a single layer across the denuded cornea and the reëpithelized areas soon develop a double layer of cells. Frequent mitosis is noted in the region of repair. The endothelial cells also show evidence of repair. These cells become enlarged and spindle-shaped. They migrate individually so that at times there is a considerable space between the most advanced and next cell (fig. 5).

Mitotic figures (fig. 6) are also observed in these cells, a finding which is exceedingly rare in the normal endothelium. The stromal cells adjacent to the lesion, which up to this time have shown only an increase in basophilic staining, slight enlargement, and an increase in their protoplasmic processes, now

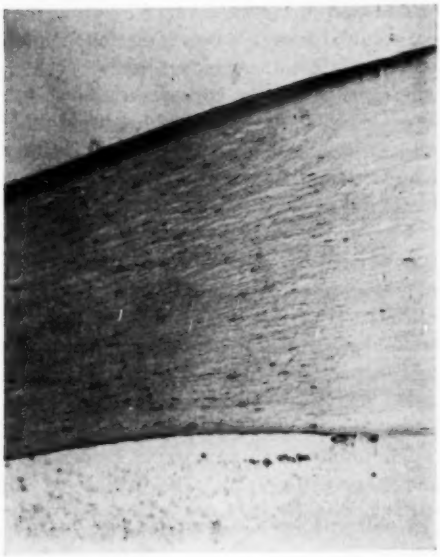

Fig. 3 (Maumenee and Kornblueth). Central freezing of rabbit's cornea (6 mm./3 sec.) 12 hours after injury, showing margin of lesion. (Hematoxylin-eosin stain. ×125.)

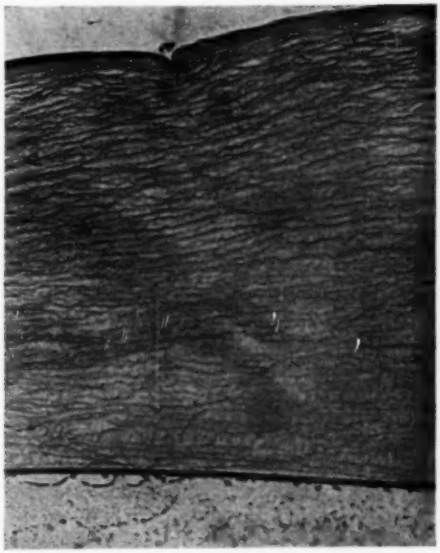

Fig. 4 (Maumenee and Kornblueth). Same cornea as in Figure 3, showing slightly more central area of the lesion. Notice complete absence of cells and edema of stroma. (Hematoxylin-eosin stain. ×125.)

show definite evidence of migration. Some of these cells become round and are difficult to differentiate from wandering macrophages with hematoxylin and eosin stain. Other cells become more spindle in shape with long protoplasmic processes. Mitotic figures can frequently be seen in the cells adjacent to the acellular area.

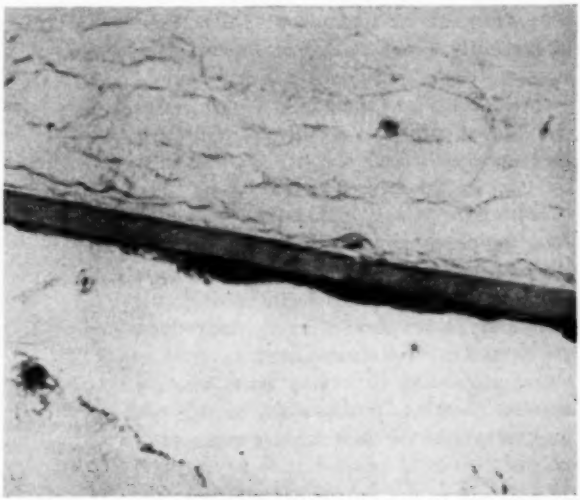

Fig. 5 (Maumenee and Kornblueth). Central freezing of rabbit's cornea (6 mm./5 sec.) one day after injury, showing migration of endothelial cells. (Hematoxylin-eosin stain. ×500.)

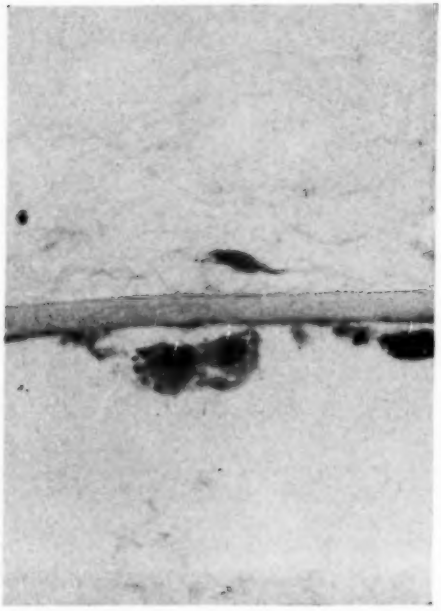

Fig. 6 (Maumenee and Kornblueth). Central freezing of rabbit's cornea (6 mm./3 sec.) 36 hours after injury, showing endothelial cell in mitosis. (Hematoxylin-eosin stain. ×500.)

Polymorphonuclear cells are conspicuously rare as they have been during the whole course of these lesions. Small monocytes however become rather prominent in the conjunctiva at the limbus and can be seen in the normal corneal stroma and near the edge of the lesion. Occasional large monocytes can also be found in the conjunctiva and normal cornea. It is difficult to differentiate these cells from the stromal cells near the edge of the injured tissue.

During the next 12 to 24 hours, the epithelium completely covers the damaged area of the cornea. The endothelial cells continue to migrate over the injured region and usually completely cover the lesion by four days. At first these cells are round or oval in shape protruding like many knots into the anterior chamber. Within a day or so, however, they resume their regular rectangular shape.

The cells in the stroma continue to invade the acellular area in a very irregular manner, some cells advancing far ahead of others. These cells vary in appearance. Some are long and spindle-shaped, with one or more nuclei; others look like small and large lymphocytes; and still others like wandering histocytes or macrophages.

Frequent mitotic figures (figs. 7 and 8) can be seen but there are not enough cells in mitosis to account for the reparative process. The occurrence of multinucleated cells would suggest that division in some instances takes place by amitosis.

By 5 to 7 days after injury, cells have invaded the full extent of the injured area. Their number and appearance however are not normal (fig. 9). The edema of the stroma rapidly subsides about this time,

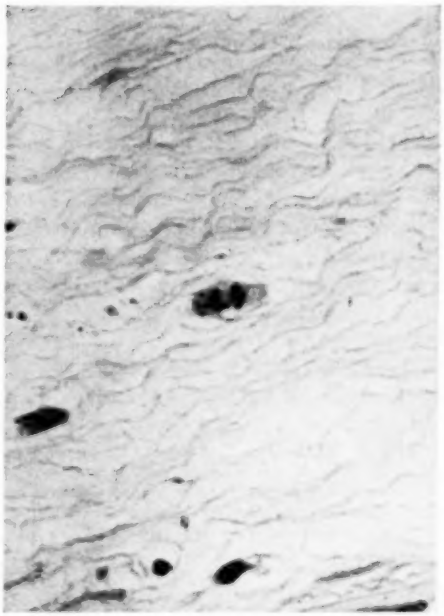

Fig. 7 (Maumenee and Kornblueth). Central freezing of rabbit's cornea (6 mm./5 sec.) three days after injury, showing corneal stromal cell in mitosis (anaphase). (Hematoxylin-eosin stain. ×500.)

and by 7 to 8 days the cornea is usually normal in thickness.

The new stromal cells gradually resume their normal appearance and number and, by 10 to 12 days, the cornea appears entirely normal. At no time during this process is there any disruption or disturbance of the corneal lamellae. Vascularization of the cornea did not occur in any specimen.

The above description of destruction and repair of corneal cells was obtained from central injuries of the cornea. Lesions made in the periphery of the cornea show similar changes except for a slightly greater invasion of leukocytes and occasional invasion of the stroma for 1 to 2 mm. by small capillaries.

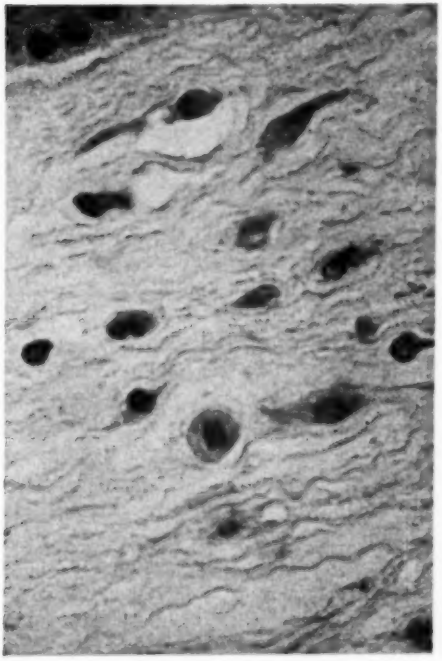

Fig. 8 (Maumenee and Kornblueth). Central freezing of rabbit's cornea (6 mm./3 sec.) seven days after injury, showing mitosing (metaphase) and regenerating corneal stromal cells. (Hematoxylin-eosin stain. ×500.)

Fig. 9 (Maumenee and Kornblueth). Central freezing of rabbit's cornea (6 mm./5 sec.) seven days after injury, showing newly formed stromal cells. (Hematoxylin-eosin stain. ×125.)

It is difficult to study the mode of death in the stromal cells in vertical sections of the rabbits' corneas because, frequently, the complete cell cannot be seen in a single section. Full thickness preparations of rabbits' corneas stain too deeply to allow them to be studied in toto.

Three-mm. strips of rats' corneas which had been frozen for 3 seconds and removed at various times after freezing were therefore prepared. The staining technique used was similar to that described by Buschke, Friedenwald, and Fleischmann.[23] In these preparations the full thickness of the cornea could be studied under the microscope.

It is found that, after freezing a 2-mm. area of the cornea for 3 seconds, definite fragmentation of the nuclei of the stromal cells can be seen 2 hours after injury (fig.

10). The first evidence of nuclear change is an agglutination of the chromatin into a single large clump or into many small clumps. The diffuse homogeneous staining of the nucleus becomes lighter and the clumps become more intensely basophilic. These clumps frequently migrate to the margin of the nucleus and the remainder of the nucleus becomes so pale that it can be seen only with difficulty.

Some of these cells then burst and liberate their granules while others shrink so the nuclei look like bits of string with 3 to 4 knots tied in it. A similar change has been observed in the stromal cells following injury by mustard and nitrogen mustard gases.[24] By 10 to 12 hours after freezing, all of the stromal cells had disappeared from the rats' corneas in the area of injury.

Fig. 10 (Maumenee and Kornblueth). Diagram of nuclear fragmentation of corneal stromal cells of rat's cornea after freezing of cornea (2 mm./3 sec.). (1) Nucleus of normal keratocyte. (2 to 6) Various stages of nuclear fragmentation.

Several interesting conclusions were obtained from these histologic examinations.

1. The stromal cells are destroyed by nuclear fragmentation following freezing.

2. Remarkably little inflammatory reaction accompanies extensive destruction of corneal cells after this type of injury.

3. All of the cells in the full thickness of a 6-mm. area of the cornea can be destroyed and stromal cells will regenerate without leaving any residual opacity of the cornea if the lamellae are not disturbed.

4. The corneal stromal cells appear to regenerate from the undamaged stromal cells and from wandering macrophages in non-perforating injuries. It was not possible to determine to what extent either of these two types of cells participated in the regeneration of the stromal cells nor was it possible to determine with certainty whether or not only one of these two types of cells was the sole source of the newly formed corneal corpuscles. In order to answer these latter questions further experiments were devised to study the source of the regenerated stromal cells.

Further experimental studies

Participation of macrophages in regeneration of keratoblasts. A macrophage has been defined by Maximow and Bloom[25] as a cell which is capable of taking up particulate matter, and storing foreign substances brought to it in colloidal solution. The simplest criteria for deciding whether a cell of the connective tissue or blood is a macrophage is the elective storing of colloidal vital dyes. The concentration of the dye must be weak for even epithelial cells will become filled with dye granules in concentrated solutions.

It is not our purpose to enter the controversial discussion of either the nature or the origin of these cells. It will suffice to mention that the macrophages participate in the phagocytosis of foreign material and repair of damaged tissues in the body. They may originate from mitotic division of preëxisting fixed or wandering macrophages, by hypertrophy and development of lymphocytes

and monocytes, and by direct assumption of phagocytic activity of cells having mesenchymal potencies of development.

Tissue-culture studies of monocytes, macrophages, and fibroblasts indicate that these cells are not fundamentally different from one another but merely various stages in development of the same basic type of cell. Carrel and Ebeling[26a, b] have shown that by varying the culture media and environmental conditions tissue cultures of monocytes, macrophages, and fibroblasts may be converted from one type of cell to another.

Ebert and Florey[27] have observed the transformation of monocytes into fibroblasts in vivo by punching holes in rabbits' ears and inserting glass chambers into these areas. These chambers then became filled with blood clots. The macrophages of the blood stream were tagged by systemic injections of vital dyes (Pontamine sky blue, trypan blue, and vital new red). By the use of microphotography and microscopic examination through the glass window they were able to observe the invasion and transformation of the tagged monocytes into fibroblasts in these blood clots.

The ability of macrophages or wandering tissue histiocytes to change into fibroblasts is now generally accepted. The corneal stromal cells do not differ markedly from fibroblasts elsewhere in the body for they are derived from the same embryonic source and have the same morphologic appearance. It is, therefore, probable that damaged corneal corpuscles are replaced in some instances by macrophages originating outside of the cornea. In order to test this hypothesis the following experiments were devised.

Rabbits weighing approximately 2 kg. were injected intravenously or subcutaneously with 45 cc. per kg. of a 1-percent trypan blue solution divided into three weekly injections of 10 cc. each.

Twenty-nine corneas were injured by freezing and the eyes were removed after 3 to 30 days, fixed in Zenkers solution, imbedded in paraffin, sectioned, and stained with lithium carmin. In all eyes, trypan-blue granules were found in extravascular macrophages in the conjunctiva and iris.

The damaged corneas could be divided into two groups depending on the number of cells containing trypan blue. In corneas with dry-ice injuries at the limbus and with complete injuries, from 50 percent to 75 percent of the cells contained dye granules

Fig 11. (Maumenee and Kornblueth). Freezing (3 sec.) of whole cornea of rabbit saturated with trypan blue, 21 days after injury. Showing trypan blue granules in corneal stromal cell. (Lithium carmin stain. ×750.)

in the regenerated area. In the corneas with central lesions only a very occasional cell was found containing the dye.

In the early stages of repair, the tagged cells were round and looked like wandering macrophages. After complete recovery had occurred, the dye-containing cells in the stroma looked like otherwise normal corneal corpuscles (fig. 11). These cells were scattered evenly through the previously damaged area.

In 15 control animals saturated with trypan blue in which the corneas were not frozen, the dye was never found in the corneal stromal cells. This experiment indicated that macrophages participated in the replacement of stromal cells in peripheral and extensive injuries of the cornea but they had little to do with the repair of central lesions.

The presence of trypan-blue granules in the stromal cells cannot be considered as absolute evidence that macrophages are transformed into stromal cells, for it was possible that macrophages containing trypan blue could have entered the cornea and, at a later time, either died or expelled their granules which were then phagocytized by the stromal cells.

Stokes[28] has shown that trypan blue injected into the anterior chamber is phagocytized by the stromal cells if the posterior surface of the cornea is injured. Therefore the above experiments are suggestive but they cannot be considered as complete proof that macrophages replace injured corneal corpuscles.

In another group of rabbits in which half of the cornea was injured, it was noted that the new stromal cells appeared as rapidly from the limbal side, where there were no corneal corpuscles, as they did from the corneal side. This occurred before cells were found in the central portion of the lesion so the new keratocytes could not have originated from corneal cells. It was also noted that central 6-mm. lesions of the cornea healed only 1 to 2 days more rapidly than did 3-mm. injuries around the entire periphery of the cornea. The area of the peripheral lesions is approximately 4 times that of the central one, so if only the stromal cells participated in the repair, and the cells did not divide at a greater rate due to more extensive injury, it should have taken considerably longer for the peripheral lesion to heal.

Finally, as more extensive lesions were found to heal without residual damage to the cornea, it was thought that absolute proof of participation of cells from outside of the cornea could be obtained if all of the stromal cells were killed. To this end whole corneas were frozen by repeated applications of the metal cylinders.

Frequently these corneas became vascularized and edema persisted in the dependent portions of the cornea for 2 to 3 weeks. Some of these corneas ulcerated in the lower portions and healed with rather dense scars. However, in many of the corneas the superior portion regained its normal clarity except for a light vascularization. The failure of these corneas to heal as well as the less extensive lesion was thought to be due to the extensive destruction of the endothelium or to the destruction of some essential substance in the normal stroma.

It had been noted previously in routine histologic studies of the central lesions that the endothelium recovered more rapidly than did the stromal cells. It was, therefore, thought that if one half of the cornea was frozen, and after an interval of two days the other half and one millimeter of the originally damaged cornea was frozen, it would be possible to destroy all of the stromal cells and at the same time leave undestroyed some of the more rapidly migrating endothelial cells.

The boundary of the upper and lower half of the cornea was established by making a superficial scar in the cornea with the point of a hypodermic needle, and the two halves of the cornea were frozen as described.

Histologic examinations of corneas injured in this manner revealed that either all of the stromal cells were killed or not more than 1 or 2 percent of the cells remained in the posterior central 2 mm. of the cornea.

Regeneration of the stromal cells occurred from the periphery and was similar to the repair of other less extensive peripheral lesions of the cornea except for slightly more inflammatory reaction. Approximately two weeks after injury, the corneas fre-

quently appeared normal clinically but, on histologic examination, the stromal cells were still not normal in number, distribution, and size (fig. 12).

In most instances the corneas regained a normal histologic appearance about three weeks after operation. In a few eyes the peripheries of the corneas for about 1 or 2 mm. were invaded by blood vessels. The response of the regenerated stromal cells was normal to a second injury by freezing and these corneas supported corneal grafts as well as did normal eyes.

It may be concluded from these experiments that cells other than normal stromal cells can participate in the regeneration of keratocytes. These cells probably are the monocytes of the blood stream or the fixed macrophages of the limbal tissues which have been activated by the injury.

Participation of stromal cells in regeneration of keratoblasts. Experiments devised to prove that the stromal cells are a source of regenerating corneal corpuscles have not been as conclusive as those demonstrating the participation of the macrophages. However, some observations have been made which strongly suggest that the corneal corpuscles contribute to the replacement of the destroyed cells.

In the experiments previously mentioned, in which the animals were saturated with trypan blue, only an occasional cell containing the dye was found in the regenerated damaged area if only the center of the cornea was frozen. This is in contrast to a relatively large number of dye-containing cells found in peripheral and whole injuries of the cornea.

Secondly, in lesions in the periphery of the cornea, where half of the cornea was frozen, migration of cells and mitotic figures were found on the stromal side of the lesion before an appreciable number of wandering cells had passed through the normal cornea to reach the edge of the lesion.

Indirect evidence that the corneal corpuscles might be a source of the regenerating cells is the fact that stromal cells can be cultivated in tissue culture. These cells have the same morphologic appearance as do the cells in the intact cornea (figs. 13 and 14). While these findings are not absolutely conclusive they suggest that the stromal

Fig. 12 (Maumenee and Kornblueth). Regeneration of corneal stromal cells nine days after freezing of whole cornea of rabbit, showing regenerated epithelium and endothelium. Slight edema of stroma, newly formed corneal stromal cells. (Hematoxylin-eosin stain. ×125.)

cells do aid in the reparative process of corneal lesions.

These experiments demonstrate that all of the cells in the full thickness of the cornea may be destroyed and, if the lamellae are not disrupted, the cornea will regain its normal clinical and histologic appearance after several weeks. The keratoblasts which replace the destroyed stromal cells originate from the remaining keratocytes and wandering macrophages from outside of the cornea.

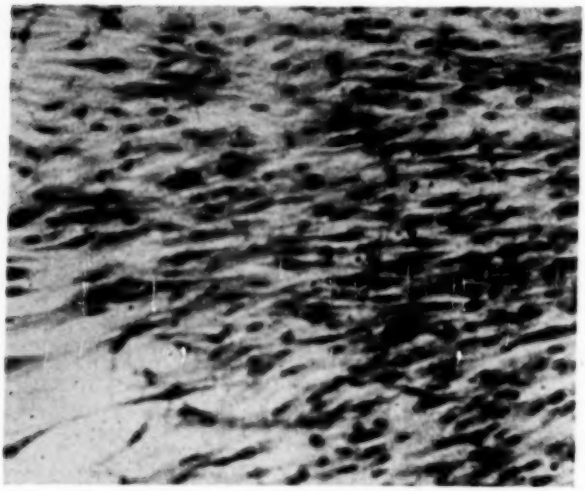

Fig. 13 (Maumenee and Kornblueth). Tissue culture of normal stromal cells of rabbit's cornea. (Giemsa stain. ×125.)

It is clear then that, if one is to establish with certainty whether or not the stromal cells in a donor corneal graft are replaced, both the keratocytes in the grafted cornea and the macrophages of the recipient animal, or the stromal cells of the donor cornea, must be tagged.

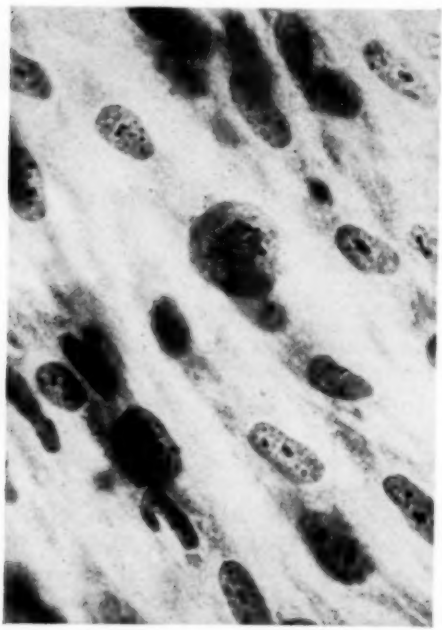

Fig. 14 (Maumenee and Kornblueth). Tissue culture of normal stromal cells of rabbit's cornea, showing mitosis (metaphase). (Giemsa stain. ×500.)

The problem of tagging these cells is not an easy one for it must be remembered that any foreign substance introduced into the donor cells may be expelled and be phagocytized by the recipient cells if the donor cells are injured or destroyed.

Summary

Previous investigators have suggested that the destroyed corneal stromal cells may be replaced by migration and multiplication of undamaged corneal corpuscles and by invasion of cells from outside of the stroma. Most of the evidence set forth by these workers has been based on routine histologic studies. In this report, the mode of repair of various-sized lesions has been described in which all of the cells in the full thickness of the cornea have been destroyed by freezing. This type of lesion causes very little inflammatory reaction and, when the injury has been completely repaired, the cornea appears normal on both clinical and histologic examination.

It has been shown that keratoblasts can be derived from two sources in nonperforating lesions of the cornea: (1) The macrophages or fixed-tissue histiocytes which have been stimulated to migrate by injury to the cornea, and (2) the activated normal corneal cells. Nonirritating lesions in the center of the cornea are repaired primarily by undamaged stromal cells. Similar lesions in the periphery of the cornea are repaired by wandering macrophages and undamaged stromal cells.

These findings indicate that, if it is to be proven whether or not the stromal cells are replaced in a donor corneal graft by tagging the cells of the recipient, it will be necessary to identify both the keratocytes and macrophages. Of course, it may be possible to solve this problem by tagging only the stromal cells of the donor cornea.

Conclusions

1. Rabbits' corneas will regain their normal clinical and histologic appearance after most, if not all, of the stromal cells have been destroyed by freezing.

2. The stromal cells die by nuclear fragmentation after freezing.

3. Destroyed corneal stromal cells are replaced by migration and multiplication of undamaged corneal corpuscles and by a transformation of wandering macrophages.

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Ophthalmic Miniature

To George Whatley

Passy, May 23, 1785

. . . By Mr. Dollond's saying, that my double spectacles can only serve particular eyes, I doubt he has not been rightly informed of their construction. I imagine it will be found pretty generally true, that the same convexity of glass, through which a man sees clearest and best at the distance proper for reading, is not the best for greater distances. I therefore had formerly two pair of spectacles, which I shifted occasionally, as in travelling I sometimes read, and often wanted to regard the prospects. Finding this change troublesome, and not always sufficiently ready, I had the glasses cut, and half of each kind associated in the same circle. . . . By this means, as I wear my spectacles constantly, I have only to move my eyes up or down, as I want to see distinctly far or near, the proper glasses being always ready. This I find more particularly convenient since my being in France, the glasses that serve me best at table to see what I eat, not being the best to see the faces of those on the other side of the table who speak to me; and when one's ears are not well accustomed to the sounds of a language, a sight of the movements in the features of him that speaks helps to explain; so that I understand French better by the help of my spectacles. . . .

B. Franklin

A FURTHER, VERY DELICATE TEST FOR ASTIGMATIC AXIS, USING THE CROSS CYLINDER WITH AN ASTIGMATIC DIAL AND WITHOUT USE OF LETTER CHARTS*

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The purpose of the procedure as to astigmatic axis proposed in the paper presented by Crisp[1] at the meeting of the American Ophthalmological Society in 1942 was to afford a delicate control test for axis in astigmatic errors, especially of low amount, in which the test for axis with cross cylinder and test letters seemed insufficiently definite and reliable. That test utilized the wagon-wheel type of astigmatic dial, more particularly the axis chart either of Lancaster and Regan or of Verhoeff.

In the course of the preliminary clinical and photographic studies in relation to that test for axis, it became obvious that several other astigmatic dials might yield interesting results along the same lines, and brief consideration was given to the use of a rotating single cross for the purpose.

Stine proceeded to devote further attention to these possibilities, and later reported to Crisp his studies and observations. From these Stine had evolved the new test, which Crisp now proposes shall be known as the "Stine test for astigmatic axis." Both of the present writers have continued to employ this new test during the past 2 or 3 years, and have found it more definite and freer from complications than any other test known to them.

The new test is of surprising delicacy and simplicity, although like other subjective tests it demands full understanding and cooperation on the part of the patient. Like Crisp's test it is generally used as a control after preliminary testing for axis with the cross cylinder and the letter chart, and in the light of any evidence which may be furnished by ophthalmology, skiascopy, or an astigmatic dial. In the larger astigmatic errors it may not have to be resorted to at all, although even here it may sometimes clear up doubts. In the small astigmatic errors (to which some workers pay little or no attention, but which may be quite important) it is most valuable.

The rotating cross is most conveniently and expeditiously used with a pulley mechanism for remote control from the examiner's chair near the patient, although some refractionists will rely (less conveniently) upon the services of an office helper for changing the position of the lines of the cross. Ophthalmologists who refract with a mirror and laterally inverted charts will, of course, have their charts within arm's length. The only disadvantage of the test as compared with the combined use of cross cylinder and letter charts or wagon-wheel chart is that, for absolute accuracy, the position of the rotating cross should be changed with each change of axis of the cylinder in the trial frame, although a discrepancy of a few degrees in the placing of the cross lines is usually of little practical importance.

At each step of the procedure, the lines of the rotating cross are made to straddle exactly the axis of the correcting cylinder in the trial frame. That is to say, the two lines of the dial should stand at 45 degrees to either side of the axis of the trial cylinder. The cross cylinder, usually the 0.12D. or the 0.25D., is held so that its axes correspond with the two axes of the rotating cross (that is at 45 degrees with the axis of the trial cylinder), and the cross cylinder is turned

* Presented before the Section on Ophthalmology, American Medical Association, Chicago, June, 1948.

or "flipped" in the same manner as in testing for axis with the letter chart.

The patient is asked to say with which position of the cross cylinder the two lines of the rotating dial appear more nearly matched as to blackness or sharpness, or with which position of the cross cylinder there is the lesser amount of contrast between the two lines. The cylinder in the trial frame is then moved toward the corresponding axis of the cross cylinder (plus toward plus, minus toward minus) in the position which gives greater uniformity of the lines or the lesser contrast between them.

If the choice has been made, and the position of the lens in the trial frame is changed, the position of the rotating cross must also be changed so as to straddle exactly (or at least approximately) the new position of the axis of the trial cylinder.

The final stage of the test is reached when the patient insists that the variation of emphasis, or the reversal of sharpness or blackness from one line to the other, is equal in both positions of the cross cylinder; and, as under the test with cross cylinder and letters, the patient's accuracy may be cross-examined by turning the trial cylinder to each side of the selected position and repeating the test.

The patient may occasionally misunderstand the test and may answer paradoxically. Like other tests, this one is usually more reliable in the absence of active accommodation, although sometimes less accurate if the patient's vision is appreciably fogged. The use of a slightly over- or under-correcting trial cylinder affects the accuracy of the test practically not at all, although a slight over-correction may often increase its sensitivity.

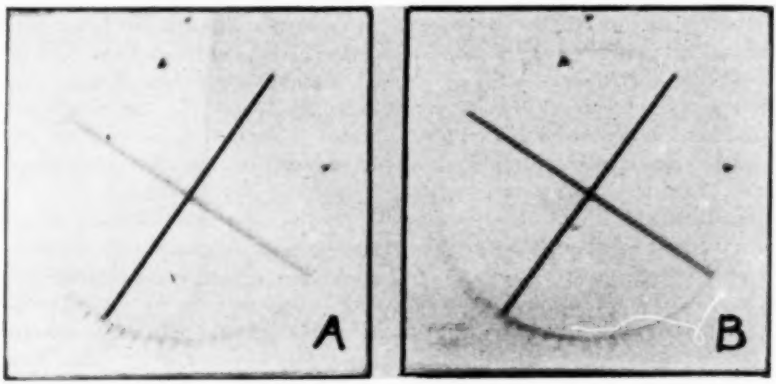

Fig. 1* (Crisp and Stine). Basic error of camera lens, rendered astigmatic, represents a final need for correction with +1.0D. cylinder axis 90°. For these two photographs the correcting +1.0D. cylinder had been placed inaccurately with its axis at 80 degrees. The two lines of the rotating cross were set respectively at 35 and 125 degrees. The cross cylinder was first placed with its plus axis at 35 degrees, and then with its plus axis at 125 degrees. The choice as to relative uniformity is obviously for the second of the two positions, indicating that the correcting plus cylinder should be turned toward 90 degrees. Astigmatic difference between the two lines in A is 0.59D., and in B, 0.09D.

* *Note as to illustrations.* For definiteness of illustration the basic error of the camera lens was that of mixed astigmatism, requiring a final correction with −0.25D. sph. ⊂ +1.0D. cyl. ax. 90°, and the 0.12D., cross cylinder (−0.12D. sph. ⊂ +0.25D. cyl.) was used. In actual practice it will be found that similar sharp differentiation by the patient is usually obtainable with such a weak cross cylinder and when dealing with a correcting cylinder as low as 0.25D.

The astigmatic differences between the two lines of the dial in the meridians shown in the illustrations were determined by the use of Percival's[3] equation for obliquely crossed cylinders and the law as to square of the cosine.

Very occasionally, determination must be made between conflicting results as to the use of this test and the use of letters with the cross cylinder. But, generally speaking, the test with cross cylinder and rotating cross is as delicate and reliable as any procedure in refractive work, or more so.

It seems worth while to point out that, subject to spherical measurements, it is possible to accomplish all the measurements (axis and strength) for astigmatism by means of the rotating cross, without resort to the letter chart. As demonstrated by Crisp in 1917,[2] the rotating cross may be

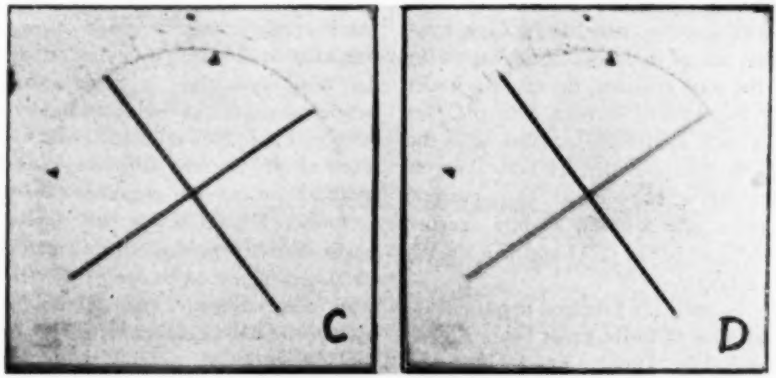

Fig. 2 (Crisp and Stine). For this pair of photographs the correcting +1.0D. cylinder had been inaccurately placed with its axis at 100 degrees. the cross was set with its lines at 55 and 145 degrees respectively, and the cross cylinder was held with its plus axis first at 55 degrees and then at 145 degrees. The choice is obviously for the former position, indicating that the axis of the correcting plus cylinder should be turned toward 90 degrees. Astigmatic difference between the two lines is 0.09D. in C, and 0.59D., in D.

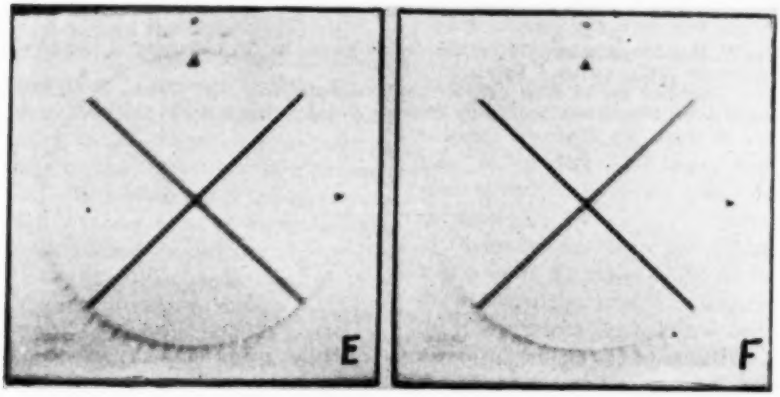

Fig. 3 (Crisp and Stine). For these two photographs the correcting plus cylinder was placed with its axis in the proper position, namely at 90 degrees. The rotating cross was placed with its lines respectively at 45 and 135 degrees, and the cross cylinder was held with its plus axis first at 45 and then at 135 degrees. There is obviously no choice as to the "equal inequality" of sharpness of the two lines on the rotating cross, indicating that the correcting cylinder is now at the proper axis. Astigmatic difference between the two lines is 0.25D. in both E and F.

conveniently used in combination with a low cross cylinder for extreme refinement as to the exact fraction of astigmatism.

For this purpose, the axis having been determined, and the cross having been rotated so that one of its lines coincides with the axis of the trial cylinder, the cross cylinder (usually the 0.12D.) is held with the plus or minus axis alternately parallel with the axis of the trial cylinder. If both lines of the cross are actually equal, each position of the cross cylinder will slightly sharpen one of the lines of the cross and will slightly blur the other.

Thus, the patient's selection may be made to discriminate as to the error being slightly above or slightly below an exact eighth of a diopter of astigmatic difference. If the patient's response is paradoxical, all that is necessary is to inquire which position makes the two cross lines more equal in sharpness. The definiteness of this test may, of course, be vitiated by the presence of irregular astigmatism.

As to the axis test which is the main topic of this paper, a further application of the same principle may be made during determination of the axis by cylinder skiascopy. In this application, a cross cylinder of proper strength (as demonstrated by experience in the individual case) is held with its axes at 45 degrees with the axis of the cylinder before the patient's eye, and the examiner decides which way there is less suggestion of uncorrected astigmatism. But, as stated in regard to use of the test at the trial case (subjective test), in most patients, except those with larger errors or amblyopic eyes, such doubts may be settled more expeditiously and more conclusively along subjective lines.

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Ophthalmic Miniature

To evert the upper lid grasp the eyelashes between the thumb and index finger of the left hand and draw the lid down towards you, pressing the center of it back with the handle of your sound before the eye is opened and the lid released. It will then be everted so that its inner surface is fully exposed for accurate, deliberate and complete treatment.

The everted lid should be gradually returned to its proper place; do not allow it to snap back suddenly—a bad practice

Memorandum Book of a Tenth-Century Oculist
Translated by Casey A. Wood.

FIXATION DISPARITY AND THE FUSIONAL PROCESSES IN BINOCULAR SINGLE VISION*

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INTRODUCTION

We have two eyes, therefore two retinal images, but we experience ordinarily a single perception of space. The normal physiologic and psychologic means through which this phenomenon takes place are called the fusional processes.

If, while one is looking at a distant object, a prism, base-out (for example), of not too high power is suddenly interposed before one eye, momentarily two objects are seen. These two, however, immediately move rapidly toward each other, the speed seeming to increase as the separation becomes less, as though each were attracted to the other by a magneticlike force. Then they suddenly coalesce, the final single impression giving no hint of its dual character. This phenomenon is said to illustrate the compulsion for fusion, a reflex to prevent diplopia. Under this compulsion eye movements occur such that the eye behind the prism turns to fixate the image of the object now seen through the prism. The movements of the eyes necessary for the reunification of the images are known as fusional movements. As usually stated, once the attention is directed to a given object the reflex to fusion so directs the pointing of the eyes that the images on the two retinas will fall on corresponding retinal elements or as near as possible to those elements. When this has taken place, one assumes that the neural excitations that arise from the two eyes are transmitted as "cortical" images to identical centers or regions of the visual cortex where unification takes place, the unification occurring prior to the conscious awareness of the perception.

The ophthalmologist needs a measure of the strength of the compulsion to fusion as an indication of the efficiency of the binocular visual mechanism and its ability to cope with muscle imbalances. The only measures available are the so-called prism vergences or fusional amplitudes. In the test for these, the eyes of the patient are directed to a target and then forced to converge (or diverge) by means of prisms placed before the eyes, base-out (or base-in). The prism power in each case is gradually increased until the patient reports a doubling of the target. At this report the prism power is noted. The findings so obtained for the convergence and the divergence are used as a measure of the fusional ability of the patient. Sometimes the prism strengths at which "blur" occurs and at which fusion is regained are also considered. Attempts are made to relate these data to the degree of lateral heterophoria present and finally to the ocular comfort of the patient.

That prism vergences are, at least in part, measures of the fusion ability is clear, since the fusion reflex cannot be separated from the convergence mechanisms and since it must demand particular muscular synergies of the oculorotary muscles of the eyes. However, it is questionable whether fusion power alone is being measured.

In prism vergence tests, probably three variables are involved: (1) The degree of the forced convergence (or divergence), (2) the strength of the fusion compulsion reflex, and (3) the degree to which the otherwise normal accommodative-convergence reflex is altered or embarrassed. The stimulus to accommodation (the target distance) is constant throughout the test.

* From the Mayo Clinic. Read at the meeting of the Milwaukee Oto-Ophthalmic Society, Rochester, Minnesota, May 8, 1948.

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The introduction of prism power before the eyes ordinarily sets up a stress in the normal accommodative-convergence reflex relationship, as long as the images remain fused. An accommodative change demanded by the changed convergence does not occur because of the compulsion to maintain clear vision, and it has been shown that over fairly wide limits the accommodative change in these tests is small, except as the prism strength approaches the diplopia point.[1]

In the prism vergence test it is the increasing stress in the convergence-accommodation reflex together with that of the musculomechanical processes which is pitted against the compulsion for fusion as prism power is increased. Diplopia occurs either when that stress is so great as to overcome the reflex innervation to maintain single binocular vision or when the mechanical limits of the oculorotary muscles are reached. Certainly, there is an expenditure of energy involved, and also a fatiguing of the muscles in the process. Both the magnitude of this stress and the strength of the fusion compulsion will undoubtedly vary from individual to individual.

Experimental evidence indicates that in spite of the compulsion to register the dioptric images of the two eyes as near as possible on corresponding retinal points, there occur an actual small deviation of the eyes and a corresponding slipping of the cortical images, although fusion is still maintained.

Identical target patterns observed on the two sides of the stereoscope will appear under normal conditions single, and then the images of these patterns are said to be "fused." Dissimilar (and unfusable) details *centered* on each of the same two patterns will under certain conditions appear decentered, that is, will appear displaced relative to each other, in spite of the fusion of the images of the identical patterns. This displacement occurs especially when the observer is heterophoric, or when the convergence and its normal corresponding stimulus for accommodation are altered. This phenomenon has been designated a *fixation disparity* (formerly, a "retinal slip") because the evidence indicates that the retinal images of the point of fixation may be actually disparate.

While this phenomenon may be a common observation among those who use the stereoscope or haploscope, it was Lau[2] who first described and correctly interpreted it while performing experiments on a different problem. He did not recognize any relationship between it and phoria.

He used targets, as illustrated in Figure 1A, in a haploscope, before the left and right eyes. Each target consisted of a long central line and a pair of shorter parallel lines that extended only to the center of each target. On one, the two short lines could be adjusted laterally by means of a screw, and the displacement could be measured by a scale and vernier. While the observer fixated the central line, and its images were fused, Lau adjusted the one pair of lines until the two opposing ones appeared in alignment. In every case, he found that both lines had to be displaced a small distance in the *same* direction. The magnitude of the displacement increased somewhat if the convergence of the arms of the haploscope was increased.

The interpretation given was that the true chief rays for the corresponding elements at the foveas of the two eyes were actually diverging slightly behind the position of the fused central line, the line of fixation.

Hofmann[3] reported the lag in the pointing of the eyes with rapid movements of the arms of the haploscope. Also, in commenting on Lau's work he expressed the belief that the phenomenon was associated with the interference in the normal accommodation-convergence reflex.

Lewin and Sakuma[4] set a playing card on each side of the haploscope; a four of diamonds before one eye and a five of diamonds before the other as illustrated in figure 1D. On looking into the haploscope the observer easily fused the images of the

four outer diamonds. The central diamond seen by only one eye, however, appeared decentered with respect to the outer four, especially as the convergence of the arms of the haploscope was changed.

In 1928, under the designation of "retinal slip," Ames and Gliddon[5] reported experiments with the haploscope in which targets (fig. 1B or fig. 1C) were used. They were able to show that the direction of the displacement of the small discs within the larger ones was generally the same as the direction of the phoria of the observer. Also, they found a fair correlation between that convergence of the haploscope arms necessary to eliminate the displacement of the discs, and the magnitude of the phoria measured under the same conditions. The close similarity of the results from the two types of targets suggests that the phenomenon occurs irrespective of whether the fusion is in the central or in the more peripheral parts of the binocular visual field.

In the use of the eikonometer with the direct comparison targets (fig. 1E),[6, 7] it is a common observation that for the average patient who has heterophoria the opposing arrows seen by the left and right eyes on each side of the binocularly observed center appear displaced in the same direction. In fact, this displacement appeared to be a contributing factor to the lowered precision of measurements in the horizontal meridian, compared to those in the vertical, especially at the reading distance. The apparent magnitude of the displacement cannot be predicted, however, by the degree of the phoria.

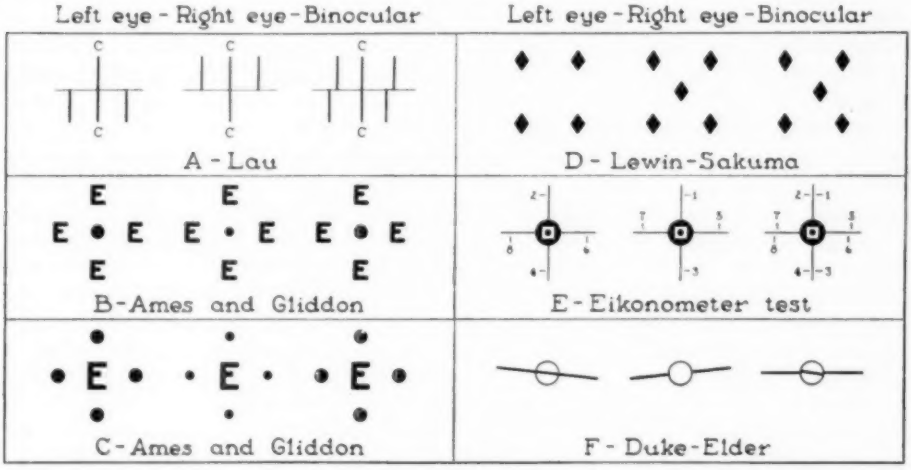
Left eye - Right eye - Binocular
A - Lau
Left eye - Right eye - Binocular
D - Lewin-Sakuma
B - Ames and Gliddon
E - Eikonometer test
C - Ames and Gliddon
F - Duke-Elder

Fig. 1 (Ogle, Mussey, and Prangen). Types of targets used by different authors for haploscopic observation with which fixation disparity was evident.

Duke-Elder[8] illustrates a pair of targets (fig. 1F) which show that this same phenomenon can also occur as a cyclotorsional displacement of the monocular images compared to the binocularly fused portions of the targets.

This phenomenon rests on the well-known fact that disparate images in the two eyes can be fused, if that disparity is not too great, that is, if they fall within the so-called Panum fusional areas.[9] These areas increase with peripheral angle; they are 6 to 10 minutes of arc near the macula. Disparate images are those which do not fall on corresponding retinal elements of the two eyes. Images which fall on corresponding points of the two eyes give rise to the ex-

perience of the same *primary* subjective sense of direction, as though each eye were used alone.

Were it not for the existence of the fusional areas, physiologic diplopia (or, better, double images) could be demonstrated for all images of objects in space which did not fall exactly on corresponding retinal points. Thus, in the fusion of disparate images, where a single sense of direction is experienced, that subjective direction must be a compromise between the primary directions associated with the two noncorresponding retinal elements on which the two disparate images are falling.

Objects in the binocular visual field which are so arranged (for example, by haploscopic, Polaroid, or red-green glass methods) that they can be seen only by one eye are experienced in a subjective direction corresponding to the primary uniocular organization of the retinal elements on which the images fall, unless those images are near other images of binocularly seen contours the images of which are fused.[5]

Therefore, if the eyes tend to overconverge or overdiverge, owing to innervations or mechanical stresses ordinarily manifested as a phoria when the eyes are disassociated, they could actually deviate from exact fixation, so that the images of the point of fixation would be disparate to an extent limited by the size of Panum's fusional areas. The subjective direction of the fused images of the point of fixation would be a compromise between the two foveal elements in the two eyes on which the images fell as in normal stereoscopic vision. Objects in the field of view seen monocularly would be seen in the subjective direction according to the primary characteristic of the retinal elements on which the images fell.

That this is actually the case is illustrated by data that have been obtained for the longitudinal horopter[10] as determined by the nonius method. In Figure 2,* the eyes fixate a point on an object at F. On either side a number of narrow vertical rods are so mounted that they can be moved nearer or farther along fixed tracks. Before the eyes is placed a special illuminated screen with apertures cut out in such a way that, except for the fixation object F, the upper halves of the rods are seen by one eye, and the lower halves are seen by the other eye. All the rods are properly shielded from the surroundings and are observed against a uniformly illuminated background. As any rod is moved along its track the two halves of the rod appear displaced laterally relative to each other, the apparent displacement changing with the position of the rod. The observer adjusts the position of each rod until the two halves appear collinear, that is, in the same subjective direction. The rod at this position, then, by definition, has images in the two eyes that stimulate corresponding retinal meridians. Experiment shows that generally the esophoric subject tends to set all the rods in a curve that lies entirely in front of the point of fixation (fig. 2a), while the exophoric subject tends to set all entirely behind the point of fixation (fig. 2b). Thus the images of the point of fixation are actually disparate, uncrossed in the first instance and crossed in the second.

The phenomenon of fixation disparity, which is found in a majority of subjects, implies that the cortical images arising from the two eyes are actually slipped or displaced a small amount with respect to each other. The angle of fixation disparity is a measure of the degree to which the images have slipped, in the same sense that Panum's area, although measured as a retinal dimension, pertains to a cortical area within which disparate images are fused. The processes involved in the compulsion for fusion normally strive to keep the images from the two eyes as nearly as possible on corresponding points. The phenomenon of fixation disparity shows, however, that the fusion is not exact when a tendency for a disassociation exists (a heterophoria), although the unification of the images is preserved.

* In these figures, for simplification in representation, the angle of fixation disparity is shown as though originating in only one eye.

Fixation disparity as a measure of the displacement of the cortical images will depend on the strength of the innervations and stresses of heterophoria, the strength of the fusion processes themselves, and the amount and complexity of the detail in the binocular field of view.

The purpose of this paper is to report a series of systematic measurements of the fixation disparity as influenced by a number of factors. The experiments were prompted by the thought that the fixation disparity might be an estimate, if not an actual measure, either of the strength of the fusional reflex or conversely of the strength of those forces—innervational, anatomic, and so forth—which tend toward an incorrect pointing of the eyes, while the images of the two eyes are actually fused.

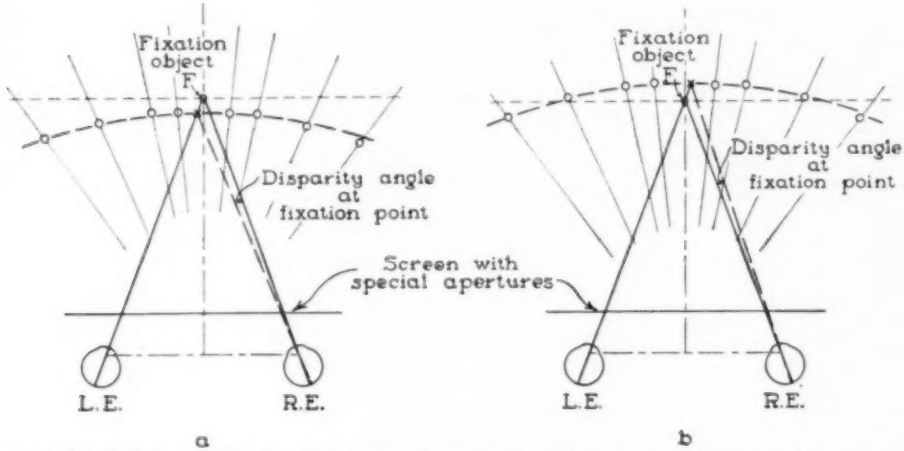

Fig. 2 (Ogle, Mussey, and Prangen). Schematic representation of horopter experiments which show that the point of fixation may not have images that fall on corresponding points.

Present experiments

Distant-vision test

Instrumentation. On an aluminum-coated screen, set up 2.5 meters from a subject's eyes, patterns and special test configurations were projected by suitable lanterns (fig. 3). The subject observed the screen through a phorometer, to which had been attached a pair of Polaroid plates (5-cm. square) before the two eyes with the planes of polarization at right angles to each other. This Polaroid attachment could be turned down out of a field of view, and the two plates could be interchanged before the eyes if desired. The target for fusion stimuli consisted of Snellen letters projected by a lantern, the total field subtending an angular size of about 20 degrees. A small central area of a given size could be blanked out at the center of the target and thus appear black to the subject. The size found convenient is a square that subtends a visual angle of about 1.5 degrees to the subject. With this center no stimuli for fusion are present within the foveal regions of the two eyes, but details for fusion exist everywhere outside this area.

The test configuration was projected on the blank square at the center of the screen by a second lantern into which a special slide arrangement had been built. The test details (see insert in fig. 3) consisted of a horizontal bright line, 28-cm. long and 5-mm. wide, and a pair of opposing (vernierlike) short vertical bright lines (arrows), 2.3-cm. high and 2-mm. wide (2.5 minutes of arc).

The arrows were polarized by Polaroid

film in the slide, so that one arrow would be seen by one eye and the other by the second eye, when viewed by the subject through the Polaroid plates. The upper arrow was fixed (stationary) but the lower could be displaced horizontally by means of a special mechanical arrangement in the lantern, which was operated by a screw and knob on the outside.

The displacement of the two arrows was read by the experimenter from an accurate dial indicator on the lantern, to an estimated 0.2 minute of arc (angle subtended to the subject), which is well within the maximal sensitivity found. By means of a shutter arrangement, the lower arrow could be occluded or flashed onto the screen at the will of the operator.

A light-green filter could also be placed over the upper arrow, if needed for making the identification of the arrows easier for the subject. The long horizontal line prevented fusion of the arrows and possibly reduced any tendency for a vertical deviation.

The general illumination of the room was kept subdued, and the luminosity of the screen and fusion detail were the same throughout the experiments. The binocular visual field was restricted wholly to the details on the screen.

Procedure. The phorometer is adjusted to the subject's head so that the eyes are centered. With the Polaroid plates before the eyes, the visual acuity of each eye is checked by means of the Project-O-Chart, the test target being projected on a screen. After this the phoria is estimated by the Maddox rod and also by the double prism test, a spot of light being projected on the screen in a room totally dark.

The target (with the 1.5-degree square) and the test arrows are then projected on the screen. With the Polaroid plates removed (both eyes observing the target), a determination of the dial reading is made for which the arrows appear in alignment, as well as of the least perceptible displacement (a measure of the precision) that can be detected. The operator instructs the subject

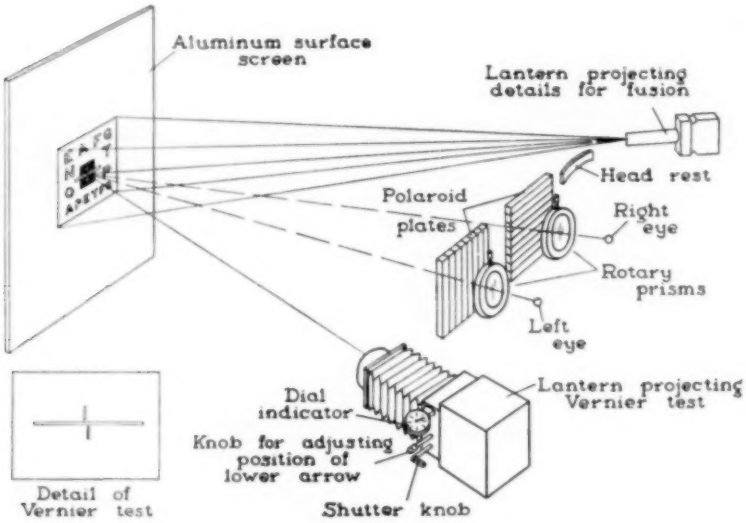

Fig. 3 (Ogle, Mussey, and Prangen). Perspective drawing of the instrumentation used to measure fixation disparity.

to look at the upper arrow, and then he flashes the lower arrow for a fraction of a second, after which he asks the subject whether that arrow was to the right of, to the left of, or was centered with the upper arrow. Between flashes the lower arrow is displaced to a new position. By the method of limits the average midpoint and precision are determined. The zero of the dial indicator is then adjusted to that reading for position and the limits can be found within which he reports that the two arrows appear aligned. The actual displacement of the arrows is expressed by the angle, in minutes of arc, subtended at the eyes of the subject.

The experiment then proceeds by the determination of the fixation disparity for different values of prism power introduced by Risley rotary prisms* before the patient's eyes. For most subjects the prism power

TABLE 1

TYPICAL DATA OBTAINED ON THREE SUBJECTS SHOWING THE MAGNITUDE OF FIXATION DISPARITY, σ, (MINUTES OF ARC) AND THE PRECISION OF THE MEASUREMENT FOR VARIOUS DEGREES OF FORCED CONVERGENCE AND DIVERGENCE; CENTRAL SQUARE 1.5 DEGREES

Prism power	Subject F. M. 1.5$^\Delta$ exophoria		Subject W. A. P. 6$^\Delta$–8$^\Delta$ esophoria		Subject K. N. O. 2$^\Delta$–3$^\Delta$ esophoria	
	σ	Limits	σ	Limits	σ	Limits
Zero	0	±0.7	6.6	±1.7	2.7	±1.3
4$^\Delta$ B.O.*	−0.8	±0.7	3.3	±1.7	2.0	±1.0
2$^\Delta$ B.I.	2.3	±0.7	8.3	±1.7	6.0	±1.3
8$^\Delta$ B.O.	−2.0	±1.0	2.3	±2.7	1.7	±1.3
4$^\Delta$ B.I.	1.7	±1.0	23.3	±2.3	15.0	±1.7
12$^\Delta$ B.O.	−2.7	±1.0	−0.7	±1.0	2.3	±1.3
6$^\Delta$ B.I.	5.0	±1.0	30.0	±3.0	21.7	±5.0
16$^\Delta$ B.O.	−4.0	±1.3	−1.7	±1.7	1.3	±0.7
8$^\Delta$ B.I.	6.3	±1.7	Diplopia		Diplopia	
20$^\Delta$ B.O.	−5.7	±1.3	−4.0	±3.3	1.3	±1.0
10$^\Delta$ B.I.	13.3	±2.3	Diplopia		Diplopia	
24$^\Delta$ B.O.	−6.0	±1.7	−11.7	±3.3	1.3	±1.3
12$^\Delta$ B.I.	Diplopia		Diplopia		Diplopia	
28$^\Delta$ B.O.	−7.3	±2.0	Diplopia		1.0	±1.7
32$^\Delta$ B.O.	−9.6	±3.3			0.7	±1.0
36$^\Delta$ B.O.					0.0	±2.7
40$^\Delta$ B.O.					−1.7	±1.0

* B.O. = base-out; B.I. = base-in

which the subject reports that the arrows are in alignment. This procedure eliminates the constant personal and instrumental errors. Only small variations between subjects are found.

The Polaroid plates are raised and the operator checks that the right eye sees only the upper arrow and the left sees only the lower arrow, and that ghost images are absent. By means of the shutter the lower line is then exposed for short intervals of about 0.25 second, and the subject is asked to judge whether this arrow was right or left of the upper arrow, or even with it. By adjusting the amount of displacement, and obtaining the patient's response, the average was placed alternately base-out and base-in; the base-out in 4$^\Delta$ steps and the base-in in 2$^\Delta$ steps. The alternation of base-out and base-in procedure was found necessary to avoid cumulative effects.

Thus, while following to some degree the procedure in the test for fusional amplitudes, here one measures any deviation of the eyes

* It is unfortunate that rotary prisms introduce optical distortion. However, the advantages of the continuously adjustable prism power over the fixed steps of loose prisms, the axes of which are also difficult to adjust accurately, outweigh the possible disturbing effects of the distortion. Cursory experiments showed that this distortion had no significant effect on the measurements, in spite of the fact that theoretical arguments might anticipate such effects.

from their positions for exact fusion that may occur during the procedure. The change in the actual deviation during the test provides new data for studying the fusional processes as the eyes are subjected to parity and the limits within which the arrows appeared aligned are given. The direction (sign) of the deviation is taken as positive if it indicates an overconvergence of the eyes and as negative if the deviation

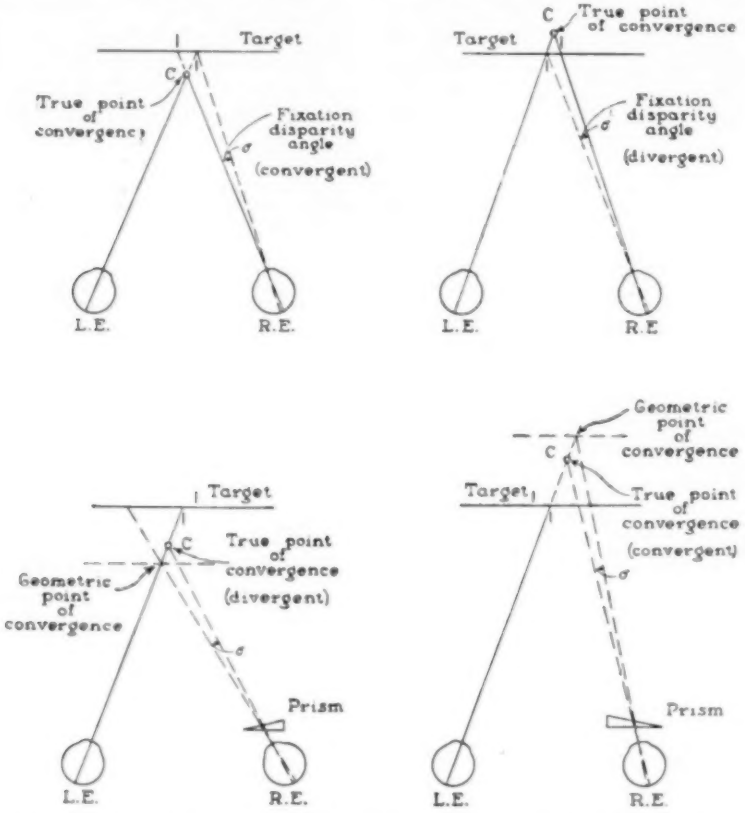

Fig. 4 (Ogle, Mussey, and Prangen). Relationship between the displacement of the polarized arrows, when they appear aligned, and the existence of an overconvergence or underconvergence of the eyes (fixation disparity).

changes in convergence by prisms and changes in the stimulus to accommodation by lenses.

Results. Typical data obtained are given in Table 1, and with others are illustrated in figures which follow. In the first column of the table, the prism power used is listed in the order in which the data were taken. In the two columns for each subject, the corresponding measure of the fixation disparity and the limits within which the arrows appeared aligned are given. The direction (sign) of the deviation is taken as positive if it indicates an overconvergence of the eyes and as negative if the deviation indicates an underconvergence (overdivergence), that is, positive if the eyes are actually converged in front of the target or the geometric position of that target when prisms were used and negative if actually converged behind the target. Figure 4 illustrates schematically the positions of the arrows when they appear aligned, and the patient overconverges or underconverges relative to the target fixated. When prisms are used

before the eyes, of course, the images of the targets are so displaced that the eyes must converge or diverge if fusion is to be maintained.

The results of eight subjects are shown in Figures 5 and 6. In these graphs, the positive for convergence and negative for divergence. The measured fixation disparity in minutes of arc is plotted on the ordinate, being taken as positive if the deviation of the eyes is convergent and negative if divergent. It is evident that a large proportion

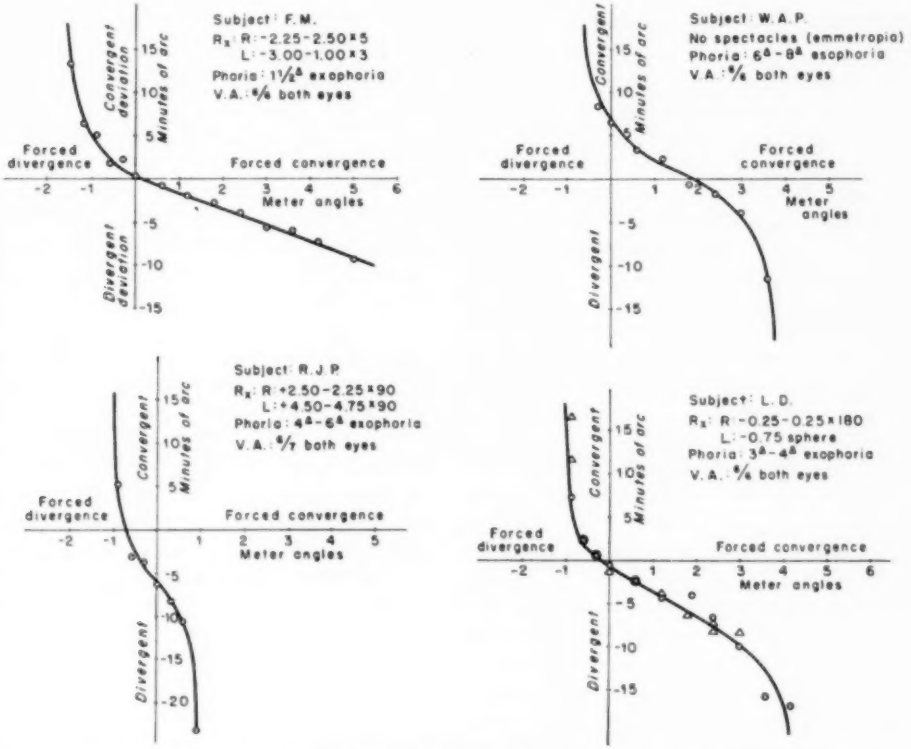

Fig. 5 (Ogle, Mussey, and Prangen). Typical data of subjects for whom the fixation disparity changes with forced convergence and divergence caused by the prisms before the eyes.

difference in the angle of convergence caused by the prisms compared to that for the 2.5-meter observation distance, measured in meter angles,* is plotted on the abscissa, of all subjects exhibit a fixation disparity of different amounts, even when no prisms are used.

Inspection of Table 1 and Figures 5 and 6 shows that points representing the data for each subject describe a sigmoidlike curve, the shape of which is different for different subjects. However, two fairly definite types of curves are distinguishable. Typical graphs illustrating these two groups are shown in Figure 5 and in Figure 6.

* The meter angles are readily obtained by dividing the total number of prism diopters by the interpupillary distance (in cm.), or roughly by 6. Meter angles are to be preferred over prism diopters or centrads, for they indicate more clearly the degree of convergence, and the corresponding demand on the accommodative mechanisms of the two eyes.

Consider for discussion the data for W. A. P. in Figure 5. This subject is nearly emmetropic, with a visual acuity of 6/6 in both eyes, but shows an esophoria of 6 to 8 prism diopters for the 2.5-meter visual distance. With no prisms before the eyes (or the rotary prisms set for zero power), the two arrows had to be displaced 6.6 minutes of arc for them to appear aligned. This finding shows that the eyes were actually overconverged by 6.6 minutes of arc, which is in the same direction as the phoria.

When prisms are placed base-out before the two eyes, a convergence is necessary if fusion is to be maintained. This convergence of the eyes is made, but if the convergence-accommodation reflex is active, this convergence will be resisted because the accommodation cannot change appreciably without blurring the vision. This resistance to the forced convergence would be manifested as an exophoria or a decreased esophoria if the fusion were not present, or as a change in the fixation disparity in the direction of a divergence. Such a reaction is demonstrated in this subject.

When prisms are placed base-in before the eyes a divergence of the eyes is forced, and the reverse behavior in the fixation disparity is to be expected. Since the limits of prism vergences base-in at this fixation distance* are not large, the fixation disparity increases rapidly because the point of diplopia is quickly reached.

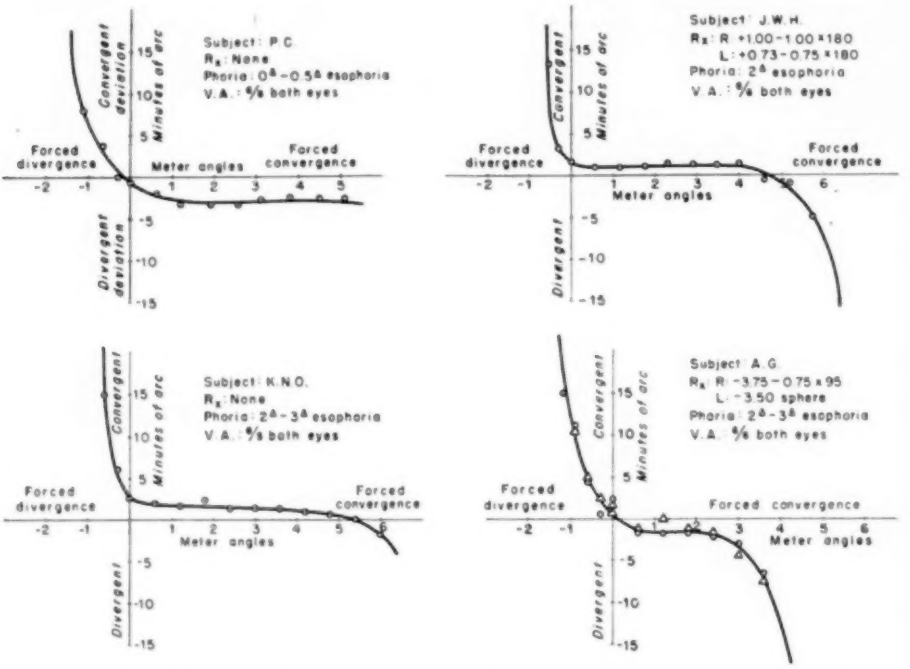

Fig. 6 (Ogle, Mussey, and Prangen). Typical data of subjects for whom the fixation disparity changes only slightly with forced convergence except at the limits of the fusional amplitudes.

* For the fixation distance b, the distance from the target to the true fixation point Δb is given sufficiently accurately by $\Delta b = b^2/2a \tan \delta$, where δ is the fixation disparity and 2a is the interpupillary distance. For a visual distance b = 2.5 meters, this distance is roughly 3 cm. for a fixation disparity of 1 minute of arc.

Considerable difference between subjects is found in the limiting prism power for forced convergence caused by prisms base-out. On approaching that point, fusion may become too unsteady for reliable measurements and diplopia may occur intermittently. In several subjects (fig. 5), the data could not be obtained to the point of diplopia because of blurring, micropsia, and the ocular discomfort associated with the sustained convergence.

Precision of the data. One of the striking aspects of these data is the smallness of the quantities being measured and the precision within which they are obtainable. As is the case in many other psychophysical measurements, the observer feels that his judgments are very uncertain, but the actual objective accuracy proves surprisingly great.

If the visual acuity is high and the muscle balance is fairly normal, it is usual to find the limits within which the two arrows appear in alignment of the order of 1 minute of arc, and often less. The precision decreases with lowered visual acuity, and decreases considerably as the degree of the forced convergence or divergence becomes large, because the relative positions of images seem more unstable and liable to change (see table 1).

Several subjects, however, showed poor precision for the entire curve, in spite of good visual acuity and low phoria. It should be clear that the limits as determined here are larger than the mean error or the standard deviation would be in other types of experimental technique.

Repeatability. Data of the nature of those described in these experiments cannot fail to vary somewhat from day to day, depending on rather intangible factors associated with the individual. For some subjects the precision of measurements seemed to vary from one day to the next for no obvious reason, although fatigue, previous excessive use of the eyes, and even disinterest may have been specific factors. However, in spite of this variation, the general curve obtained for a given subject after the lapse of several days agreed remarkably well with that previously obtained.

Figures 5 (L. D.) and 6 (A. G.) show two sets of such data identifiable by the circles and triangles. A small training effect is to be expected, but this seems to manifest itself in an increased precision and an increased amplitude of base-out prism vergence, rather than a change in the curve that represents the data. This must not be taken to imply that no changes are found, for frequently the second curve may be displaced from that taken first by a small degree, in the same sense that the phoria will change from day to day.

The particular technique used in exposing the arrow also generally had no significant effect on the curve obtained. In one technique the lower arrow was not flashed at all, the subject merely reported when he saw it to the right and when to the left of the upper arrow, as it was slowly displaced one way and then the other by the operator. The flashing technique was preferred, for it tended to reduce any alignment of the two arrows due to "desire for symmetry" and any influence of after-images, although these factors actually appeared to have only a minor effect, if any.

The small normal involuntary eye movements that are always present and which appear to increase with the stress accounted for occasional spurious responses. As the prism vergence approached the point of diplopia, fusion of the images became more uncertain, and here greater discrepancies in the repeated data were found. However, the values for the fixation disparity were already comparatively large in these regions, so that the curves themselves were only slightly modified by the variations in data. Reversing the Polaroid plates before the eyes, so that the arrows would be seen by opposite eyes, had no influence on the data.

For some subjects a second set of data obtained immediately after the first resulted in a slightly different curve. An accumulative

effect of the sustained use of prisms base-out toward the end of the test appeared to leave a residual esophoric stress evident by the vertical displacement of the curve and sometimes also by an increase in the slope (rate of change of the deviation with convergence) especially in the center of the curve. The effect may persist for several hours after the original experiment.

Care was taken not to obtain data for a curve immediately after prism vergence tests or unusual use of the eyes. In order to avoid cumulative effects during the experiment, the prisms, base-out and base-in, were alternated and frequent short rest periods were allowed. This influence of sustained base-out prisms on fixation disparity is interesting, for in obtaining prism vergence limits it is believed that the use of prisms base-out has less effect on data subsequently obtained than has the use of prisms base-in.[11]

Subject groups. An inspection of the curves selected shows rather strikingly the manner in which the subjects tend to fall into two groups according to the characteristics of the curves found. Subjects with curves intermediate between these two will probably be found, however. In the first group (fig. 5) the fixation disparity increases with the forced convergence (or divergence) of the eyes, and in the middle range the increase is almost directly proportional to the prism power. For these subjects, as the prism power is increased, the cortical images from the two eyes increasingly "slip" and the fusion of these images becomes increasingly less exact, until finally a confusion and then a diplopia occurs. Although the rate of change in the deviation with prism power suggests itself as a measure of the strength of the fusion reflex (the higher, the poorer the fusion), this is not borne out.

In the second group (fig. 6) the eyes maintain more or less the same degree of fusion, over wide ranges of forced convergence, as evidenced by the fact that the fixation disparity changes little between the limits near which sudden increases are found. The fusion of the two images for these subjects appears to be tightly held in spite of the increased prism power. Even for high degrees of forced convergence certain of the subjects showed only a small increase in the disparity (data K. N. O. and J. W. H.), until the point was reached where abrupt changes might be expected.

This second type of curve is not unexpected, for it might be anticipated that the fusional processes would hold the images tightly together during the entire prism vergence test, until a sudden giving way would occur at the limits with resultant diplopia. However, one would expect the fixation disparity to be zero between these limits. The anomalous factor shown in these data is that more or less constant actual fixation disparity is maintained between those limits. The precaution taken at the beginning of the measurements to determine the "zero" for each observer precludes the possibility that this displacement is a constant personal or instrumental error. The direction of this disparity in the level portion of the curve appears generally to be in the direction of the phoria.

Blurring the retinal images. There would be reason for expecting that the fusion in the face of opposing stresses would be more difficult when the retinal images are blurred, because all contours on which fusion will depend would be less distinct. However, it is well known that in prism convergence tests on the major amblyoscope or synoptophore the fusion of the images seems to hold well even after the images are so blurred as to be almost unrecognizable. The fixation disparity curve as obtained here also does not change appreciably when the images of both eyes are blurred by plus ophthalmic spherical lenses at distant vision or with occluder (special etchedlike) glasses.*

*These glasses were supplied by Dr. E. D. Tillyer of the Scientific Department of the American Optical Company. They consist of a series of glasses manufactured by a special process for reducing visual acuity in fixed steps.

However, if the image of only one eye is blurred, the fixation disparity does change with prism vergence, which indicates a less exact fusion. In these experiments the images were blurred by a +1.0D. sph. and the special occluder glass, both of which reduced the acuity of the eye to about 20/70. The effect of the blurring of the image of one eye on fixation disparity was somewhat different according to the two groups of subjects described previously. Figures 7 and 8 show the results obtained. In Figure 7, the curve changes markedly when the image is blurred, both for forced convergence and for forced divergence. In Figure 8, the change appears as a vertical displacement of the curve and occurs more significantly for divergence than for convergence.

Peripheral fusion. If the details for fusion are limited more and more to the peripheral

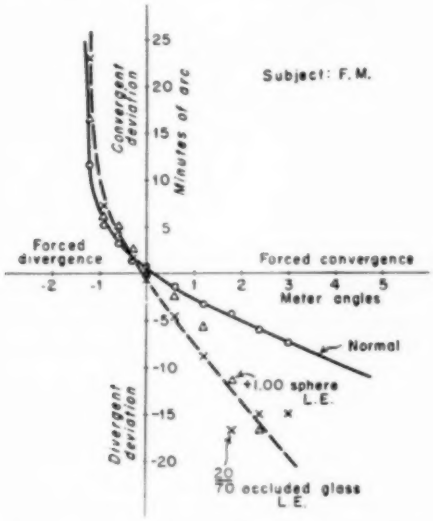

Fig. 7 (Ogle, Mussey, and Prangen). Influence of blurring the image of one eye on the fusion.

visual field, the fixation disparity curves change markedly, although again this is different in the two groups of subjects. By increasing the size of the blanked-out square in the projected fusion pattern on the screen, in the center of which the vernier arrows are seen, the images which can be fused are restricted more to the periphery of the retinas.

Voluntary eye movements do not occur,

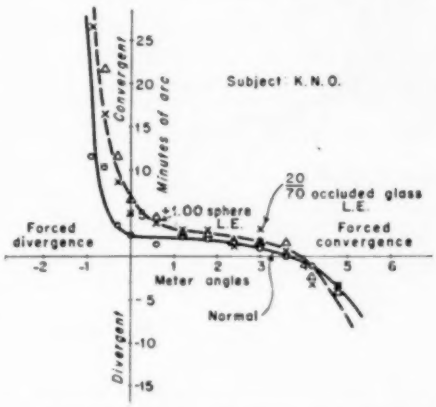

Fig. 8 (Ogle, Mussey, and Prangen). Influence of blurring the image of one eye on the fusion.

for the eyes are fixated at the center if they are to see any displacement of the arrows. Squares used to test this effect were of angular sizes of 0.75, 1.5, 3, and 6 degrees of arc subtended at the subject. The results obtained on two subjects, as examples of the two groups, are illustrated graphically.

In the first case (fig. 9) for a given convergence the fixation disparity increases rapidly as the size of the blanked-out area increases. Since Panum's areas in the periphery are many times larger than those in central vision, such increased disparity is possible while still maintaining fusion. The precision of the data decreased also. The response of this subject is entirely consistent with the previous data (compare Figure 5 for F. M.).

Figure 10 shows how peripheral fusion influences the fixation disparity in the second type of subject (compare Figure 6 for K. N. O.).

The data were obtained for the series of target sizes at each prism setting, in the same order as shown in Table 1; hence the

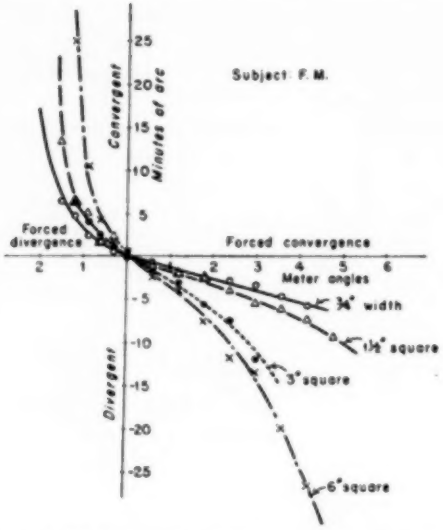

Fig. 9 (Ogle, Mussey, and Prangen). Influence of peripheral fusion on fixation disparity.

results found were not cumulative effects of the forced vergences. Again the data are consistent. The fixation disparity increases as the fusion is pushed into the periphery, but here this is evident by a vertical displacement of the curve in the convergent direction. As the forced convergence increases, the deviation then changes rather slowly toward the divergent direction.

For the subject whose data are illustrated in Figure 9, the curves for different-sized, central targets deviate even more if a red glass is used before one eye and a green glass before the other (fig. 11). This suggests that a red-green visual rivalry (such rivalry was experienced during the test) acts as a further hindrance to exact fusion.

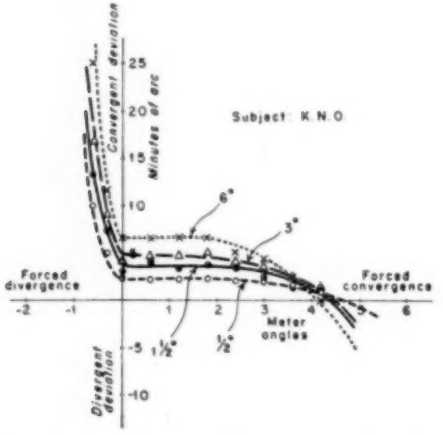

Fig. 10 (Ogle, Mussey, and Prangen). Influence of peripheral fusion on fixation disparity.

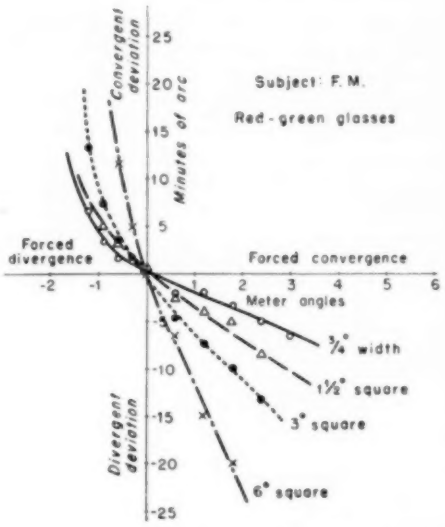

Fig. 11 (Ogle, Mussey, and Prangen). Influence of red-green glasses for different degrees of peripheral fusion on fixation disparity.

However, the red-green glasses on the second subject had only a small effect on the results obtained, and almost no rivalry was experienced.

Effect of lenses. Because the change in fixation disparity with forced convergence or divergence is probably associated with the convergence-accommodation reflex, similar changes might be expected when the stimulus to accommodation was also changed, as, for example, when spherical ophthalmic lenses are placed before the eyes. Such a

change has been reported in the displacement of the longitudinal horopter as determined by the nonius method, when plus lenses were worn by the esophoric observer. Certainly the problem being studied would not be complete without such a consideration.

The procedure was to obtain data for the curves for the fixation disparity with forced changes in the convergence while spherical lenses are placed before the two eyes, for both distant and near vision.

NEAR-VISION TEST

Instrumentation. For the near-vision tests new instrumentation was necessary. A light box with a transparency plate in front was used instead of the projector lanterns and screen. Figure 12 illustrates the apparatus schematically. The features are essentially the same as those for the distant-vision apparatus, and no further description is necessary.

The fixation distance was 29 cm. (3.4

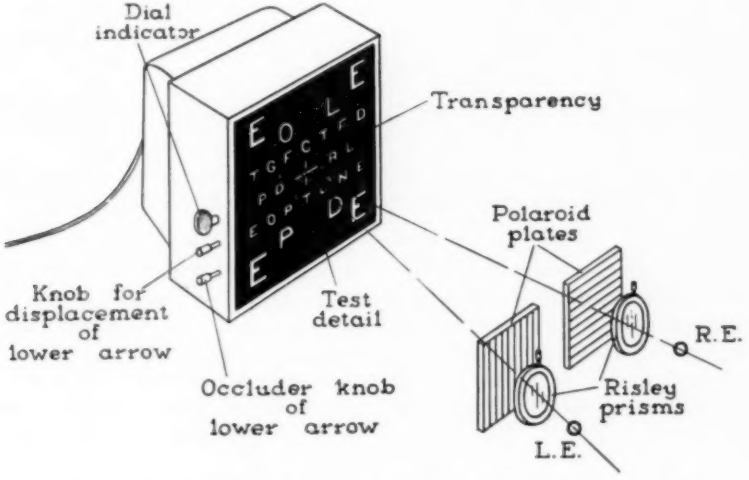

Fig. 12 (Ogle, Mussey, and Prangen). Perspective drawing of apparatus for measuring fixation disparity at near visual distances.

For distant vision, three sets of data were obtained: with the usual or with no refractive correction, and with supplemental lenses of +1.0D. sph. and −1.0D. sph. before both eyes. In each case the added sphere caused a displacement of the curves. As would be expected, the fixation disparity changes in the divergent direction with plus spheres, and in the convergent direction with minus spheres, which is in the direction that the phoria would also tend to change. The addition of the plus spheres in both cases blurred the vision somewhat, but not sufficiently to prevent data being taken, although the sensitivity was reduced.

diopters). If the subject had adequate accommodation, supplemental lenses of +2.0D. sph. and −2.0D. sph. were used, while if not, as in beginning presbyopia, supplemental lenses of +2.0D. sph. and +4.0D. sph. were used.

Characteristic curves were obtained, showing the marked influence of the stimulus to accommodation, and of the probable accommodation which took place, on the fixation disparity. Figures 13 and 14 show results of two subjects, characteristic of the two types.

It is of special interest to derive from these curves the various combinations of spheres

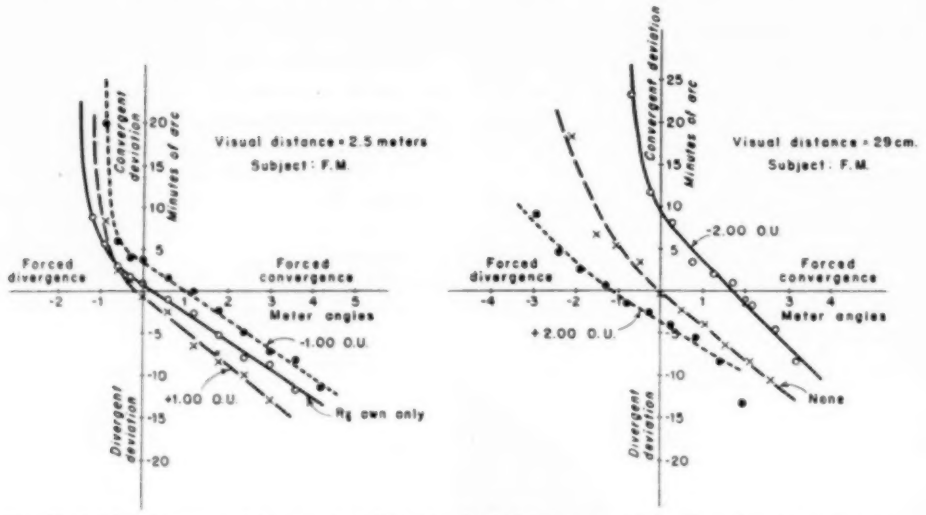

Fig. 13 (Ogle, Mussey, and Prangen). Effect of spherical lenses on the fixation disparity-convergence curve for visual distances of 2.5 meters and 29 cm.

and meter angles of convergence (prism power) each of which results in a given fixation disparity, especially a zero disparity, for then the cortical images would be exactly superimposed. Examples of such derived data are illustrated in Figure 15, for the two subjects for both distant and near vision.

In these graphs the abscissa represents the lens power and the ordinate the forced vergence—convergence positive and divergence negative. The values for forced vergence are measured from the meter angles of convergence corresponding to the distance of the target. Some inaccuracy cannot be avoided in selecting the place where a given

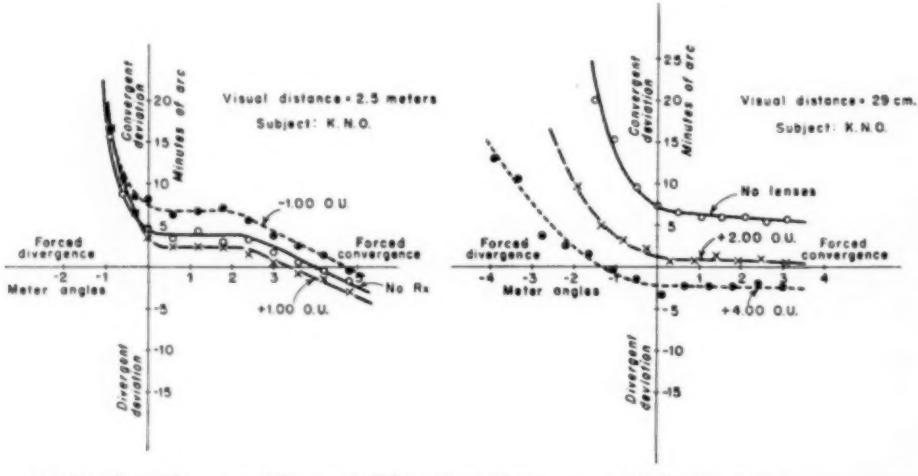

Fig. 14 (Ogle, Mussey, and Prangen). Effect of spherical lenses on the fixation disparity-convergence curve for visual distances of 2.5 meters and 29 cm.

curve in the original graph intersects the ordinate of a given fixation disparity. However, the results are not much in error.

The average slope of these lines is a measure of the comparative influence of prisms and lenses on fixation disparity and the convergence-accommodative relationship. For the two subjects illustrated here about 0.6 to 0.8 meter angle of convergence (3 to 4 prism diopters) has the equivalent effect on fixation disparity of 1 diopter of lens power before the two eyes.

The approximate parallelism of the lines in these derived graphs certainly can be taken as evidence that the fixation disparity is a specific measure of the stress of muscle imbalance during fusion. The approximate parallelism of the lines indicates also that the addition of the spherical lenses has caused in the main a displacement of the curves, that is, has added a constant factor.

At this time it is not possible to attach special significance or functional importance to the "zero" disparity line, although certainly this could be taken as the condition of no muscular imbalance and perfect fusion, and as such it would be desirable. As far as the spherical lenses are concerned, it appears that when the subject wears the proper refractive correction the fixation disparity is small, if not actually zero.

The deficiency in the experimentation reported here lies in the fact that the actual state of accommodation in any given combination of lenses or prisms can only be presumed from the presence or absence of blur (loss of visual acuity). Reliance was placed on previous experimentation by one of us, which showed that the maximal change in accommodation with prism vergence was of the order of ± 0.25 diopter, and on the literature, for the statement that the accommodation changes only very slightly for forced convergence or divergence except near the limits.

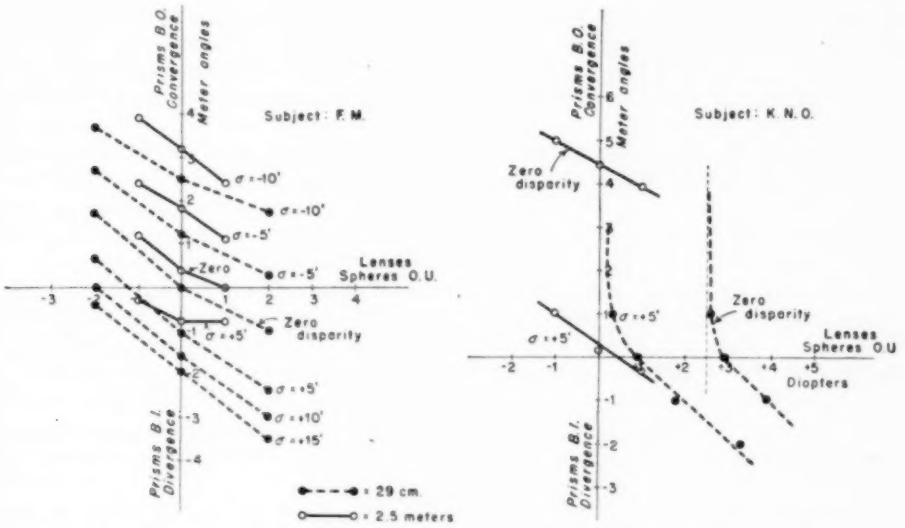

Fig. 15 (Ogle, Mussey, and Prangen). Derived data from Figures 13 and 14 showing comparative influence of prisms, forced vergence, and spherical ophthalmic lenses.

Comment

A fixation disparity can be measured in most subjects who show a heterophoria, re-

gardless of the type of fusion detail used in the target. This means, in general, that the retinal images of the point of fixation do not fall exactly on corresponding points.

Although ideally the fusion compulsion reflex strives to direct the pointing of the eyes so that the images fall as nearly as possible on corresponding retinal elements, it may only be able to keep the images within Panum's areas of fusion because of innervations or mechanical stresses which make up muscle imbalances. Thus the two cortical images arising from the two eyes will be slightly displaced or slipped with respect to each other.

By and large the direction of the fixation disparity is the same as that of the heterophoria, although apparently not correlated quantitatively with it, probably because the phoria is a phenomenon of the disassociated eyes. Fixation disparity *a priori* need not always be associated with a phoria. The stresses of dynamic muscular balance active during actual fusion may be the result not only of mechanical and tonic neuromuscular effects but also of functional innervations, all of which would not necessarily be present when the eyes are disassociated.

Occasionally, the initial fixation disparity is found in the direction opposite to the phoria, and generally this occurs in the case of a small esophoria which nevertheless exhibits a divergent deviation. The possible influence of "instrumental convergence" must not be excluded in the phoria measurement.

The subjects seem to fall into two more or less distinct groups according to the way in which the fixation disparity (cortical image slip) changes with forced convergence and divergence of the eyes. In the first group, the deviation increases with the degree of forced convergence, while in the second, the fixation disparity remains nearly constant with the degree of forced convergence or divergence, except near the limits of the fusional amplitudes. From one point of view these data indicate that in the first type, fusion is more loosely held and the cortical images are more liable to slipping than in the second type, in which the fusion is more tightly held until the limits of fusional amplitudes are reached.

The existence of a more or less constant fixation disparity in the second type is difficult to account for. In a tightly held fusion, the second type of curve would be expected, but with the greater part of the curve coinciding with the abscissal axis, that is, with the fixation disparity zero. Only near the limits of the fusional amplitudes would there be a sudden change in the curve. The measurements of the fixation disparity as the fusion details are confined more and more peripherally constitute a crucial experiment. Otherwise, it might be argued that the constant deviation in the second group might be the result of an adapted change in the sensory subjective direction, in the same sense of an anomalous correspondence, developed by a constant fixation disparity under the influence of a neuromuscular tension.

The better explanation for these results is that the stress set up in the accommodative-convergence relationship produced by the prisms differs greatly with different individuals. Here two groups could be differentiated. In the first, a real stress is caused by the prisms, in an effort to resist the forced convergence. In addition to these stresses, there must be those manifested by the phoria. In the second group, the disproportion between the accommodation and the convergence due to the prisms introduces little or no additional stress at all; there is practically no resistance to the prisms, as though the accommodation and convergence relationship was exceedingly elastic, until the degree of convergence or divergence becomes great. Thus, in spite of the forced convergence caused by the prisms, only those stresses manifested by the phoria remain as the sole source for the ocular deviation. Hence, the fixation disparity would tend to remain constant. It would tend to be constant for a given pattern of fusion detail and only

secondarily to be influenced by a change in phoria with convergence.

Since the accommodative-convergence relationship is affected by lenses, which change the stimulus to accommodation, as well as by prisms, the fixation disparity is changed by lenses. In general it appears that the fixation disparity-prism vergence curves are displaced laterally, as though the lenses merely added a constant equivalent prism vergence change. The magnitude of this equivalence is about 0.6 meter angle (3.5 to 4 prism diopters) to 1 diopter lens power, although in one case of probable convergence insufficiency this was only 0.2-meter angle (1.5 prism diopters) to 1 diopter lens power.

These results show that fixation disparity is an indication, if not an actual measure, of the muscular imbalance when the images in the two eyes are fused. The magnitude of the fixation disparity, however, will depend not only on the stress of that muscular imbalance but also on the strength of the fusional reflex processes.

These results also suggest that the therapeutic results from the prescription of prisms would be different for the two groups of subjects as well as in specific cases. In the first they might prove helpful, in the second not at all. One could argue, however, that a much tighter fusion exists in the second group than in the first.

The interpretation of the prism vergence or fusional amplitude tests should be different for these two types of subjects.

Mayo Clinic.

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ANTISTINE: A STUDY OF ITS TOXICITY ON TOPICAL APPLICATION TO THE EYE*

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Antistine hydrochloride is a relatively new antihistaminic available for topical application to the eye. The oral use of such drugs as Benadryl and Pyribenzamine for the ocular symptoms of allergy has been disappointing.[1] The probable explanation is that insufficient drug reaches the site of the allergy.[2] Antistine, developed in an attempt to overcome this disadvantage, gives promise of symptomatic relief.[1] Since Antistine was the only antihistaminic commercially available for topical application to the eye at the time of these experiments, this study was limited to Antistine.

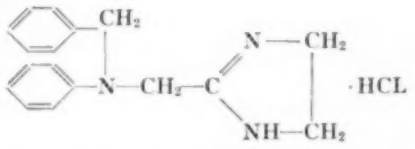
Clinical trial has not demonstrated any unusual reactions. Occasionally conjunctival congestion occurs and rarely an allergic reaction may be seen.[2a, 2b]

Recently Grant and Loeb reported on the toxicity of several different antihistaminics on the rabbit eye.[3] They studied the approximate maximum concentration at which no alteration in the rabbit cornea occurs, as shown by examination with the slitlamp, after a single drop of solution. For Antistine hydrochloride this concentration was 1.5 percent. At slightly higher concentrations, a temporary keratitis epithelialis develops. At still higher concentrations, corneal edema and loss of epithelium occurs. They found from the subjective standpoint that 0.75 percent Antistine produced the same discomfort as 0.5-percent tetracaine (Pontocaine) hydrochloride in human eyes. By altering the pH of the solutions, it was found that the discomfort was not attributable to excess acidity or alkalinity. None of the drugs produced anesthesia on the application of a single drop.

Recently Hurwitz gave the most comprehensive report of the clinical use of 0.5-percent Antistine. He found that 42 of 50 patients with various external ocular allergies obtained significant symptomatic relief.[1]

CHEMISTRY

Antistine hydrochloride† is a synthetic preparation bearing the chemical name of 2-phenyl-benzylaminoethyl-imidazoline hydrochloride. The structural formula is as follows:



The crystals are white, odorless, and have a bitter taste. Solutions for ocular application originally contained the sulfate salt and it is this product upon which Hurwitz reported.[1] It is now made as the hydrochloride in 0.5-percent concentration with a pH of 6.94 which is close to the pH of tears (7 to 7.5).[4] It is made as an isotonic buffered solution of the following formula:

Antistine hydrochloride	0.50
Boric acid powder U.S.P.	1.20
Sodium carbonate anhydrous	0.05
Potassium chloride C.P. anhydrous	0.15
Distilled water q.s.	100.00

According to Bourquin, Antistine may be combined with other substances such as penicillin, zinc, argyrol, mydriatics, and miotics.[5]

PHARMACOLOGY

A common feature of antihistaminics is an antagonism of all of the major effects of

* From the Department of Ophthalmology of the Indiana University Medical Center. Read at the Midwest Section of the Association for Research in Ophthalmology, Inc., at Saint Louis, Missouri, March 26, 1949. This investigation was supported by a grant from Ciba Pharmaceutical Products, Inc., Summit, New Jersey.

† Manufactured by Ciba Pharmaceutical Products, Inc.

histamine except its gastric secretory activity.[6a, 6b] They differ greatly in other respects. Some show an atropinelike action, while others exert a spasmogenic effect in moderate or higher doses. Certain ones augment the pressor effect of epinephrine, while others block or even reverse it. Landau and Gay in Dale tests (inhibition of guinea pig gut contractions) found that within one minute Histadyl, Bromothen, Chlorothen, Pyribenzamine, and Neoantergan completely counteracted five times as much histamine. Within one minute, Benadyl completely antagonized an equal amount of histamine, but Antistine was fully effective against only one half the amount of histamine.[7]

In experiments to counteract the effect of histamine intoxication and anaphylactic shock on guinea pigs, Antistine was again found to be the weakest of the antihistaminics tested.[8] However, no parallel existed between effectiveness against histamine in guinea pigs and their effect against human allergy.[9] Antistine is used systemically in doses larger than that of other compounds (100 mg. tablets). It was found by Gay and others to be the most effective antihistaminic against urticaria and angioneurotic edema and against dermatitis and pruritic conditions of various etiology, and it produced the smallest number of side effects (18 percent).[9]

Despite conflicting reports the consensus is that antihistaminics influence allergic symptoms by a specific antagonism of the pharmacologic effect of histamine.[6a, 10] Although there is no proof of the mechanism of action, the current belief is that they compete with histamine for the same receptor cell, displacing histamine from its point of action.[6a]

Experiment 1

Effect of Antistine on normal cornea. Since clinical trial has demonstrated an apparent lack of damage to the cornea, it was thought that a preliminary test on a small series of rabbits would be adequate before a more careful determination of its effect on the normal human cornea. It was found that staining with fluorescein was no more common in eyes treated repeatedly with 0.5-percent Antistine than in normal untreated rabbit eyes.

Effect on human cornea. Ten medical-student volunteers were selected. Both eyes of each were flushed with fluorescein and examined with the slitlamp prior to the experiment. The effect of 0.5-percent Antistine hydrochloride was compared with that of a buffered isotonic control. At intervals of one-half hour for 12 times two drops were instilled above the limbus of each eye. Antistine was used in the right eye and the control solution in the left eyes. The formula for this buffered isotonic control was:

Sodium carbonate anhydrous	0.016
Potassium chloride	0.028
Boric acid crystals	2.500
Distilled water q.s.	100.000

The pH of this solution was 5.80 and was raised to 6.94 by the addition of a few drops of concentrated sodium hydroxide. The experiments of Friedenwald and Buschke have shown that wound healing in the corneal epithelium occurs at a pH from 4.5 to 9.5.[11]

Subjective comments. Burning for a minute or two occurred after application of drops of both Antistine and the control solution but was slightly more pronounced with Antistine.

Gross objective findings. The characteristic reaction to the frequent instillation of drops was a mild to moderate congestion, mainly bulbar in distribution. It was slightly greater in the right eyes receiving Antistine.

Biomicroscopy. At the end of the day, both eyes were again flushed with fluorescein and examined with the slitlamp. In only 1 of the 10 volunteers (number 6) was any change noticed. This volunteer was an agitated "expectant" father. In the right eye treated with Antistine there were small punctate points joined to produce horizontal linear streaks below and nasal to the pupil. In the left eye treated with the control solution a

superficial punctate area, about 3 mm. in diameter, was found near the limbus at the 8-o'clock position. Since the staining was bilateral and more severe in the control eye, it was felt that some intercurrent factors were involved.

Summary. A 0.5-percent solution of Antistine hydrochloride instilled at half-hour intervals for 12 times in 10 human eyes produced no discernible corneal damage attributable to the drug. Bulbar congestion occurred in both eyes, but was slightly greater in those treated with Antistine; the subjective sensation of stinging was slightly greater in the Antistine-treated eyes.

Experiment 2

The effect of Antistine upon reëpithelization of the denuded rabbit cornea. It is generally known that agents that are noninjurious to the cornea and conjunctiva of the rabbit are equally or even less irritating to that of the human eye and that the cornea is an excellent medium to ascertain information relative to the local tissue effect of drugs.[14]

To test the possible toxic effects of Antistine upon the rabbit cornea more carefully, 30 young adult pigmented rabbits with normal eyes were selected and divided into 3 groups of 10 rabbits each. Four-percent cocaine was used for anesthesia and to loosen the epithelium. To expose and fix the eyes, they were proptosed and held between the fingers. The epithelium was then completely removed by abrasion with sterile gauze. The completeness of denudation was checked by instillation of 2-percent sodium fluorescein followed by a gentle flushing from an eye dropper with a solution of penicillin-G potassium, 2,500 units to the ml., which does not delay healing.[13] Two drops were instilled above the limbus of each cornea five times a day.

In Group I the right eyes received 0.25-percent Antistine, and the left eyes, the control solution.

The right eyes of Group II received regular 0.5-percent Antistine, and the left eyes, the control solution.

The right eyes of Group III were given 1-percent and the left eyes 2-percent Antistine.*

TABLE 1

THE DAY OF THE EXPERIMENT ON WHICH DENUDED RABBIT CORNEAS HEALED WHILE UNDER TREATMENT WITH BUFFERED ISOTONIC CONTROL OR WITH VARIOUS STRENGTHS OF ANTISTINE SOLUTION

	Drug	Day of Experiment												Average
		4	5	6	7	8	9	10	11	12	13	14	15	etc.	
Group I	Control		2	3	3	1									6.3
	Antistine (0.25%)	1	3	1	4										6.3
Group II	Control			2	4	3	1								7.3
	Antistine (0.5%)		1	1	4	2		1				1			7.9
Group III	Antistine (1%)					3	2	1	1				2		10.3
	Antistine (2%)						3			1			5		12.5

Complete denudation has been used frequently.[12-15] Other methods such as disc denudation outlined with a cork borer,[15] strip denudation outlined with double-bladed corneal knife,[16] and needle prick have been employed.[11] De Roetth objected to complete denudation because he felt that it was diffi-

* Supplied through the courtesy of Dr. F. L. Mohr and Ciba Pharmaceutical Products, Inc., Summit, New Jersey. All of the Antistine solutions were formulated to be isotonic and buffered with a constant pH of 6.94 so the only variable was the drug used. The 0.25-, 0.5-, and 1-percent strengths were made as the hydrochloride but the 2-percent strength had to be made up as the sulfate since the hydrochloride is not sufficiently soluble.

cult to be certain that one is producing constant damage.[17]

This objection has validity and is the reason for our separating Group I from Groups II and III in Table 1. The reason for this was that the day following the denudation it was obvious that the first 10 rabbits (Group I) had not been denuded as completely as the last 20, for in the first 10 the epithelium had already begun regeneration but had not in the last 20 rabbits. That this difference was not due to the drugs employed was indicated by the fact that the left eyes of Group I and the left eyes of Group II both received the same control solution. That the completeness of denudation was reliably equal within the groups was indicated by observation and by standardization upon previous rabbits and by frequent repetition of the same maneuver.

Results. The regeneration in uncomplicated cases is easily followed since the crescent of reëpithelized cornea at the limbus stands out brilliantly clear and normal against the greenish stained haze of the denuded area. The eyes were examined daily by staining with fluorescein and flushing gently with a solution of penicillin. Obvious secondary infection was rare. Only one rabbit in Group I was discarded because of delay in healing from secondary infection, while one rabbit in Group III died of intercurrent disease.

GROUP I. Except for the one discarded rabbit the corneas reëpithelized from the 4th to the 8th day with an average healing time of 6.3 days with both the 0.25-percent Antistine and the isotonic buffered control.

GROUP II. There was no significant difference in the healing time of the right eyes treated with regular clinical 0.5-percent Antistine hydrochloride (average 7.9 days) and the left eyes treated with the control (average 7.3 days).

GROUP III. Healing in Groups I and II was complicated only by a faint diffuse haze which was considered the result of superficial stromal damage at the time of denudation. The use of stronger strengths of Antistine caused greater conjunctival congestion, a definite delay in healing, and other evidence of corneal damage. This delay with 1-percent Antistine hydrochloride was moderate (10.3 days) and the corneal damage was moderate with superficial vascularization.

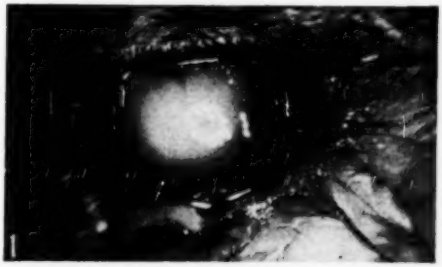


Fig. 1 (Schlaegel). Grossly relucent and vascularized rabbit cornea that had been treated with 2-percent Antistine. This cornea had apparently healed as indicated by lack of gross staining with fluorescein.

The healing time with 2-percent Antistine sulfate was pronouncedly increased (12.5 days) and the corneal damage was severe. In five of the rabbits, most of the cornea not protected by the nictitating membrane was rendered grossly relucent, densely vascularized, and very slow to heal (fig. 1).

Although clinically healed on the 15th day, microscopic sections revealed that the stroma was covered not by epithelium but by a hyaline membrane 1 to 2 times as thick as Descemet's membrane (fig. 2). Van Gieson stain indicated that the hyaline membrane was modified superficial stroma.

Summary. The use of Antistine five times a day on completely denuded rabbit corneas demonstrated that the 0.25- and 0.5-percent solutions do not delay healing over that of the control solution, but that the 1-percent and especially the 2-percent strengths are definitely toxic, resulting in delayed healing and vascularized scars.

Fig. 2 (Schlaegel). Microscopic sections revealed that the cornea had not become reëpithelized, but that the superficial stroma had developed a hyaline membrane. Degeneration, vascularization, and cellular infiltration of anterior two thirds of stroma.

Experiment 3

Effect of Antistine on the size of pupil and upon accommodation. Since some of the antihistaminics demonstrate an atropinelike, spasmogenic, or adrenergic response, it was felt necessary to check the pupil and ciliary body for signs of effect. Harris, McGavack, and Elias found that Benadryl applied topically to the bulbar conjunctiva in 0.5-percent aqueous solution produced a moderate mydriasis of readily measurable proportions which appeared within 15 minutes and became maximum within one hour.[18] The capacity for accommodation was simultaneously decreased. Benadryl enhanced the mydriasis of homatropine and lessened the miosis of eserine. However, no effect on the pupil was noted from the oral use of 400 mg. of Benadryl daily. In their studies of Antistine hydrochloride, Benadryl hydrochloride, Decapryn, Histadyl, Neoantergan, Pyribenzamine, Thenylene, and Thephorin, Grant and Loeb noted that only Benadryl hydrochloride had a noticeable mydriatic or cycloplegic effect.[3] Using Benadryl, Antistine, and Pyribenzamine, von Sallmann found that only Antistine did not weaken the miotic action of di-isopropyl fluorophosphate.[19]

Methods. Under constant conditions of illumination, the apparent size of the pupils of the 10 human volunteers previously mentioned was measured before and after the day of drop instillations. Reading was permitted during the experiment. Using a Prince rule with Duane line for test object the nearpoint of accommodation of each eye was checked 10 times both before and after the experiment by bringing the test object toward the subject to the point of blur. Since only the relation between "before" and "after" was desired the total cycloplogic error was not determined and glasses were worn only if desired.

Results (Pupil). Table 2 clearly demonstrates an absence of effect on the pupil. *(Accommodation).* Table 3 gives the results of the average value of the 10 measure-

TABLE 2

The apparent pupillary diameter in mm. of the eyes of 10 human volunteers "before" and "after" 12 instillations of Antistine (0.5 percent) to the right eyes and control solution to the left eyes

Volunteer	Right Eyes (Antistine)		Left Eyes (Control)	
	Before	After	Before	After
1	4.50	4.50	4.00	4.00
2	4.50	5.00	4.50	5.00
3	3.50	3.50	3.75	3.50
4	3.50	3.50	3.50	4.00
5	4.50	4.50	5.00	5.00
6	4.50	4.50	4.50	4.50
7	4.00	4.75	4.50	5.00
8	4.00	4.00	4.00	4.50
9	5.00	5.00	6.00	5.00
10	5.00	4.50	5.00	4.50
Average	4.30	4.38	4.48	4.50

ments of accommodation of each eye both before and after the experiment. The average for the 10 subjects indicates an increase in accommodative power of the right eyes (Antistine) of 2.3 cm. and an increase in the left eyes (control solution) of 1.2 cm., but statistical analysis indicates that none of these differences is significant.

TABLE 3

THE AVERAGE OF 10 DETERMINATIONS OF THE NEAR POINT OF ACCOMMODATION MEASURED IN CM. FOR EACH EYE OF 10 VOLUNTEERS BOTH "BEFORE" AND "AFTER" 12 INSTILLATIONS OF ANTISTINE (0.5 PERCENT) TO THE RIGHT EYES AND CONTROL SOLUTION TO THE LEFT EYES

Volunteer	Right Eyes (Antistine)		Left Eyes (Control)	
	Before	After	Before	After
1	22.7	16.4	17.9	14.3
2	16.1	16.1	15.3	16.1
3	17.0	11.5	15.2	12.6
4	9.4	8.5	9.2	9.7
5	13.0	12.9	12.8	13.9
6	13.0	12.9	13.8	12.9
7	18.7	13.7	18.1	15.7
8	13.5	14.4	12.7	10.8
9	14.7	15.6	15.9	15.7
10	17.8	10.4	14.2	11.4
Average P.P.	15.5	13.2	14.5	13.3
Standard Deviation	3.5	2.4	2.5	2.1

Summary. Antistine hydrochlroide (0.5-percent) applied as drops 12 times in one day to the eyes of 10 human volunteers failed to affect the size of the pupil or the accommodation.

COMMENT

Experimental studies of the toxicity of antibiotics on the cornea indicate that many of them, especially in the powder or ointment form, produce some damage.[12, 14–16, 20] It has also been shown that anesthetics and antiseptics commonly employed in ophthalmology are even more toxic to the cornea.[13, 21, 22] Since Antistine hydrochloride solution in 0.25- and 0.5-percent strengths did not produce corneal damage in these experiments, Antistine as commercially supplied (0.5-percent solution) should be a safe drug to add to our armamentarium.

GENERAL SUMMARY

1. Antistine hydrochloride (0.5-percent) instilled repeatedly in 10 human eyes produced no discernible corneal damage. Bulbar congestion and subjective stinging were slightly greater with Antistine than with the control solution.

2. The use of Antistine on completely denuded rabbit corneas demonstrated that 0.25- and 0.5-percent solutions do not delay healing longer than does a control solution, but that the 1-percent and especially the 2-percent strengths are definitely toxic.

3. Antistine hydrochloride (0.5-percent) applied as drops 12 times in one day to the eyes of 10 human volunteers failed to affect the size of the pupil or the accommodation.

CONCLUSIONS

These experiments indicate that 0.5-percent Antistine hydrochloride is not toxic to the cornea and does not affect the pupil or accommodation.

1040 West Michigan Street (7).

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THE EFFECT OF DICUMAROL ON THE VISUAL FIELDS IN GLAUCOMA*

A PRELIMINARY REPORT

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The problem of progressive loss of visual field following a successful filtration operation in glaucoma is one that has plagued ophthalmologists for years. The general consensus seems to be that these changes are due to an irreversible vascular process which is set up while the tension is above normal limits and has progressed sufficiently so that when the tension is reduced, either by surgical or medical means, there is no regression, but apparently a continued progression of the vascular process.

As far as can be determined, no completely satisfactory pathologic observations have been made on the ocular vascular system in early cases of chronic simple glaucoma. Duke-Elder[1] states that there is a vascular stasis and quotes three individual case reports by Levinsohn, 1908, Ronne, 1913, and Hanssen, 1918, in which all showed evidence of circulatory stasis and vascular lesions, either of periphlebitis or endophlebitis of the episcleral or vortex veins, with areas of leukocytic infiltration.

Knapp,[2] in reporting on cases of atrophy of the optic nerve with cupping and low tension, states that "atheromatous carotid arteries cannot alone cause this descending atrophy, but the condition must be caused by simultaneous circulatory disturbances in the optic nerve from arteriosclerotic vascular changes."

Best[3] called attention to the fact that arteriosclerotic changes in the small nutrient vessels may damage the optic nerve, while Siegert[4] and von Stief[5] believed that the cause of optic atrophy in cases of "pseudoglaucoma" are the result of arteriosclerotic changes in the vessels supplying the optic paths.

Gradle,[6] in discussing glaucomatous cupping and atrophy of the optic nerve in cases where the tension was never found to be elevated, held that the condition begins as a low-grade neuritis limited to the anterior third of the optic nerve, the vessel-bearing portion, and leading to an absorption of the nerve fibers, producing the cavernous changes in the nerve described by Schnabel.[7] Lagrange and Beauvieux[8] found sclerosis and obliteration of the small nutritive vessels of the nerve in several cases of primary glaucoma.

Loewenstein[9] demonstrated changes in the walls and thromboses in the small vessels of the optic nerve, producing cavernous degeneration and sclerotic plaques. He concluded that the degenerative changes found in the nerve in glaucoma are the result of vascular damage with impairment of nutrition rather than the effect of increased intraocular pressure.

It is interesting to note that the recent studies of Putnam[10] and his co-workers on the etiology of disseminated sclerosis present some evidence that vascular thrombosis has a definite bearing on the formation of the plaques found in nerve tissue in this disease. This group has recently treated a series of cases of acute disseminated sclerosis with dicoumarin and report encouraging results in those cases which are characterized by remissions and exacerbations.

Rintelen[11] has described the histologic findings in cases of arteriosclerotic atrophy of the optic nerve. He believes that sclerosis of the central retinal artery has little or no effect on the nerve and that the damage in these cases is due to sclerosis of the small nutrient vessels. Vail[12] states, "It is entirely probable that vascular disease of the nerve may account for the progress of cupping,

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atrophy, and field changes that frequently occur after the ocular hypertension has been quite controlled in true glaucoma, especially in the aged."

In view of these facts and hypotheses it would seem that the most reasonable explanation for the progressive field changes in chronic simple glaucoma is arteriosclerotic changes in the nutrient vessels of the optic nerve. These changes may involve slowing of the blood stream, narrowing of the lumen of the vessels, formation of atheromatous plaques in the endothelium, and formation of mural thrombi.

In searching for some method to treat these patients, many of whom seem to be in desperate straits, it was believed that a vasodilator might be of benefit if the vasodilatation could be prolonged. Further, it seemed that a drug with anticoagulant properties which would inhibit the formation of thrombi might possibly be of value in the treatment of these cases. The only drug which met both of these requirements was dicumarol.

Schofield,[13] in 1924, and Roderick,[14] in 1929, reported on hemorrhage disease in cattle following ingestion of spoiled sweet-clover hay. In 1939, Link[15] and his associates isolated and crystallized the active principle in spoiled sweet-clover hay that was responsible for this disease of cattle. Since that time a great number of experimental and clinical investigations have been made on 3,3′-methylenebis (4-hydroxycoumarin), better known as dicoumarin or dicumarol.

Meyer, Bingham, and Axelrod[16] reported that the administration of the chemical, either orally or intravenously, is succeeded by a protracted prolongation of the prothrombin time and coagulation time. This effect follows an initial latent period of 24 hours following administration of the drug. In therapeutic amounts no untoward symptoms were produced but excessive quantities produced spontaneous hemorrhages and fatalities in dogs.

Bingham, Meyer, and Pohle[17] first noted that the most constant pathologic change produced by the substance is a widespread dilatation of capillaries, arterioles and venules, and this finding has been confirmed by Wright and Prandoni,[18] Bollman and Preston[19] and Townsent and Mills.[20] It is of interest to note that this vasodilatation occurred in animals whether they died from overdose of the drug or were destroyed for study following therapeutic dosages.

In treating patients suffering from arteriosclerosis obliterans or thromboangiitis obliterans with dicumarol, Wright and Prandoni[18] noted an increased tendency to bleed at the site of ulceration and attributed it to the dilatation of minute vessels. Allen, Barker, and Waugh[21] believe that something in the body is necessary for the action of dicoumarin because if the drug is added to drawn blood, the prothrombin time is not affected. The bleeding time is not affected by the clinical use of the drug but the sedimentation rate is routinely increased.

The method used in administration of the drug in the cases to be reported consisted in hospitalizing the patients and, on the first day of hospitalization, the administration of 300 mg. of dicumarol by mouth.

Routine determination of the prothrombin time, according to the method of Quick[22] was started on the second day in the hospital and carried out daily thereafter. According to this method the normal prothrombin time runs around 11 to 13 seconds. By the administration of dicumarol the prothrombin time was elevated to between 35 to 45 seconds and maintained at that level during the period of hospitalization. The amount of dicumarol to be given each day is determined by the reported prothrombin time of that day. On the average it was found that after the initial dosage of the drug a daily dosage of 100 mg. was sufficient to maintain the desired level in the blood, although on occassion the dose had to be decreased or increased for a day or so.

It is of interest to note in this connection that, if there appears to be some danger of

hemorrhage, the prothrombin time can be reduced dramatically by the intramuscular injection of 50,000 units of penicillin. This will reduce the prothrombin time but will not prevent it being raised again to the desired level by the administration of dicumarol, while the intravenous use of vitamin K will not only reduce the prothrombin time but keep it at low levels for several days in spite of the continued use of the anticoagulant.

Of the nine cases to be reported in this paper, dicumarol was initially administered for a period of two weeks only. However, several patients have had a second course of the drug because, while some improvement was noted after the first course, it was felt that further improvement was desirable and consequently further treatment was advised.

The first case reported was perhaps the most dramatic of all. After the first course of dicumarol, from which there was a most striking, and to me unbelievable, response, the fields held well for a period of 10 months. At this time it was noted that there was again a marked lower nasal field cut to within 10 degrees of fixation. The patient was given a second course of the drug and one month after this the field had again become almost normal while a month later it was within normal limits and has remained so until the present, 8 months after the last course of dicumarol.

This quite naturally brings up the question as to whether it is necessary to give repeated courses of the drug and at what intervals these should be given, or whether, as in the case of some patients who have suffered thrombosis of the coronary artery, a maintenance dose of the drug should be given for some months or years. I am not prepared to answer this question definitely at the present time, although I do have three elderly patients with advanced field changes on a maintenance dose at this time. These patients all had increased intraocular pressure which was reduced by operation, but I believe that the field changes in them were more characteristic of an arteriosclerosis of the vessels supplying the optic pathways than of those which we ordinarily associate with glaucoma. It is too early to speculate what the outcome will be in these elderly patients for if, after further study, this therapy proves to be of value in treating the visual changes in long-standing glaucoma it is my belief that the older patient with advanced field changes, due in all probability to arteriosclerosis, will prove to be the most intractable type of case for such treatment.

Again, although I have not yet carried out such a procedure, I have the feeling that, if dicumarol proves to be of value in these cases, probably the most advantageous use of the drug would be its long-continued administration over a period of years with weekly checks on the prothrombin time after the blood level is finally stablized.

Case reports

Case 1. W. G., aged 44 years. This Negro was first seen on December 12, 1944, complaining of early presbyopic symptoms. He stated that the vision in the right eye had been failing for some years but he thought the left eye was all right and that all he needed was some reading glasses. There was no history of pain or congestion in the eyes at any time. Vision was: O.D., hand movements at one foot; O.S., 20/30.

External examination was negative with the exception of the pupils which were semidilated and reacted poorly. The media were clear while the fundi showed a minimal arteriolar sclerosis and a deep cupping of each disc of the glaucomatous type, the pallor of the nervehead being more marked in the right eye.

The vision in the right eye could not be improved while in the left it was improved to 20/20 by +0.5D. sph. Intraocular pressure was O.D., 29 mm. Hg; O.S., 42 mm. Hg (Schiøtz). No visual field was obtainable in the right eye while that in the left eye revealed a marked defect in both the upper and lower nasal quadrants. Pilocarpine (2 percent) was ordered to be instilled four times daily and the patient asked to report in two weeks. At this time the tension was O.D., 25 mm. Hg; O.S. 35 mm. Hg; and operative intervention was advised for the left eye.

On January 7, 1945, a modified Lagrange operation was performed on the left eye. The postoperative course was uneventful, and one month after the surgical procedure tension was O.D., 25 mm. Hg; O.S., 17 mm. Hg. From that time until the present the tension in the left eye has never been above 17 mm. Hg nor below 13 mm. Hg on repeated examinations.

However, on March 31, 1945, almost three months after operation, the field in the left eye showed a good deal more contraction, and three months later the contraction was even more marked. Following this there was a more gradual contraction of the field until December, 1946. At this time the best corrected vision in the left eye was 20/30, but it should be emphasized that at no time during the observation of this patient had the blindspot showed any variation from normal.

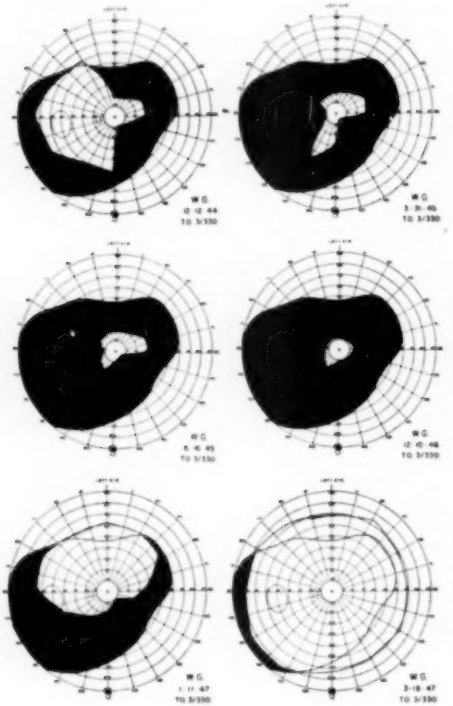


Fig. 1 (McGuire). Case 1.

Dicumarol therapy was ordered on December 12, 1946, and the patient was kept on the medication for 10 days. He was seen again on January 11, 1947, and the field was found to be much improved. Two months later, on March 15th, three months after the dicumarol therapy, he was again checked and the field found to be full in all meridians.

In June of 1947 the field remained normal and he was asked to report again in three months. On September 27, 1947, the field had begun to show a temporal contraction and a marked lower nasal quadrant cut to within 10 degrees of fixation. The blindspot remained unaffected and the best corrected vision was 20/25. At this time he was put on dicumarol for two weeks and on October 18, 1947, the field had shown marked improvement while four weeks later, on November 15th, the field had again returned to normal limits and the corrected vision was 20/20. He was last seen in February, 1948, and the field was holding well.

Case 2. M. W. P., a white man, aged 60 years, was first seen in October, 1936, when he stated that he had lost the sight in the right eye four years previously. He had not consulted a physician and came in merely to see about getting some reading glasses.

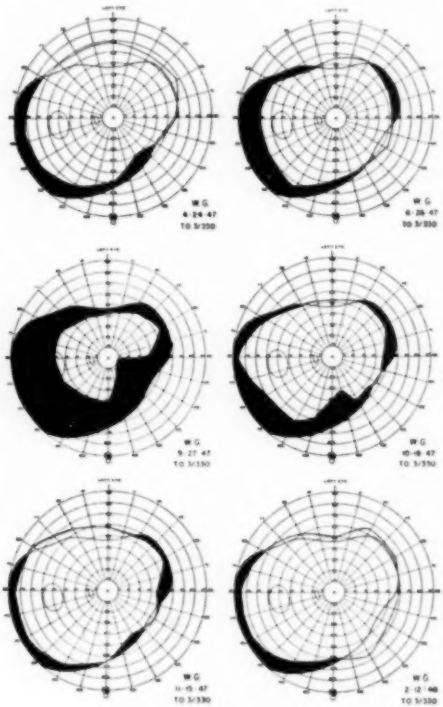


Fig. 2 (McGuire). Case 1.

There was no history of pain or inflammation in either eye. There was no light perception in the right eye while the vision in the left was 20/20.

The external examination was negative with the exception of the right pupil which did not react to light and was partially dilated. The media were clear. The fundi showed marked glaucomatous atrophy of the right nervehead and some shallow cupping of the left disc. There was a slight upper nasal contraction of the left field.

Intraocular pressure was: O.D., 48 mm. Hg; O.S., 35 mm. Hg. Pilocarpine was ordered for each eye and under this regimen the tension was reduced to: O.D., 30 mm. Hg, and O.S., 17 mm. Hg. No essential change was noted in the eyes until the middle of 1940, four years after the patient was

first seen, when, in spite of the continued use of miotics the tension began to rise slightly in the left eye. Between May and December, 1940, the tension varied between 17 mm. Hg and 35 mm. Hg in the left eye with a base curve which was showing a slow but constant increase. On December 31, 1940, a trephination was done on the left eye, following which the tension was reduced from 40 mm. Hg to 15 mm. Hg, in which neighborhood it remained for several years.

During late 1943, the patient developed an acute exacerbation of the glaucoma in the blind right eye and a complete iridectomy was performed by Dr. Louis S. Greene in January, 1944. This served to reduce the tension for only a few months and then the patient began to develop spontaneous hemorrhages from the iris in the right eye and the globe was enucleated in May, 1945. In the meantime the tension and the field in the left eye had been holding well. In August, 1946, it was noted that the field in the left eye had begun to show a little more contraction and a 48-hour tension curve was done with the highest tension recorded at 22 mm. Hg (Schiøtz).

In May, 1947, the field was found to be more contracted and the blindspot definitely enlarged. Dicumarol therapy was advised and the patient entered the hospital for this therapy on May 15, 1947. He had two weeks on the drug and, on June 24th, it was noted that the nervehead was of better color and the field was improved. On August 29th the field showed continued improvement and the blindspot was about normal in size, while the fields were maintained at the same level on December 31, 1947.

In this case the central vision in the left eye has never been worse than 20/30, corrected, and, when the patient was last seen, it was corrected to 20/20.

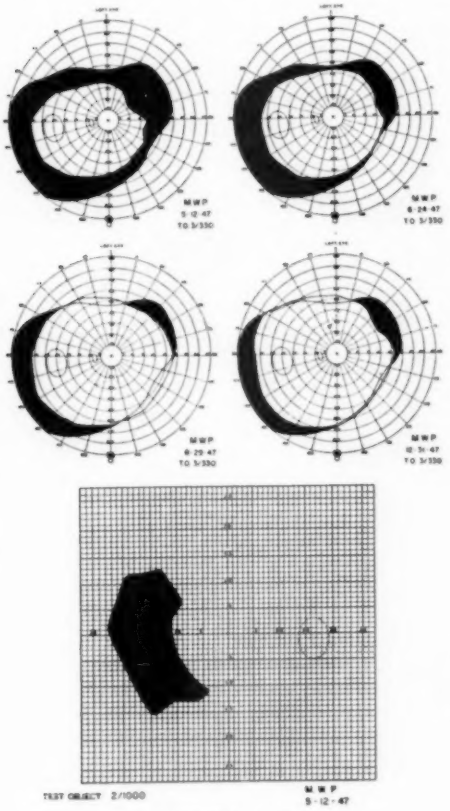


Fig. 3 (McGuire). Case 2.

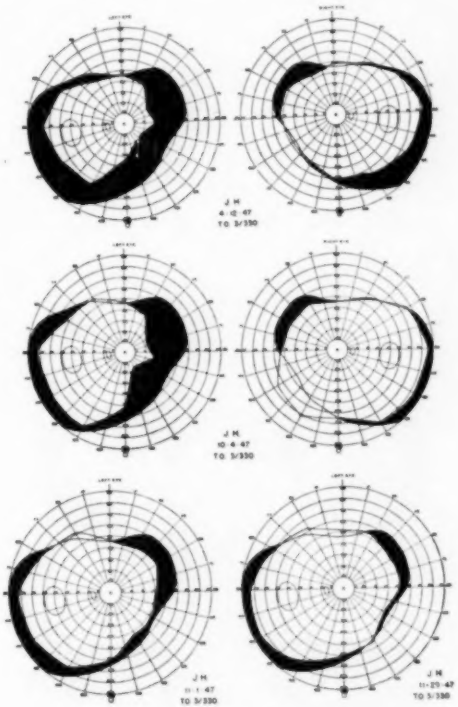


Fig. 4 (McGuire). Case 3.

Case 3. J. L. H., a white man, aged 45 years, was first seen in August, 1944, when he came to the office for a change of glasses. There was no history of ocular trouble other than the usual presbyopic symptoms. The vision was 20/20 in each eye, corrected to 20/15 in the right eye and 20/15 in the left. The external examination was negative and the media were clear. The fundi were normal with

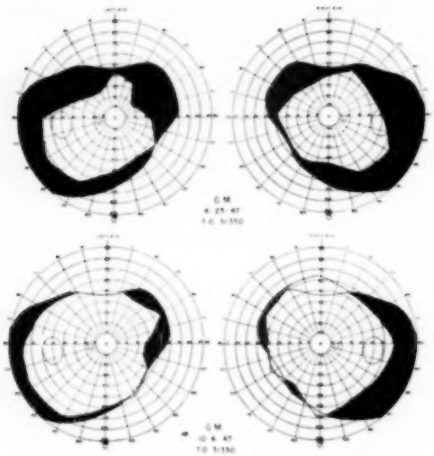


Fig. 5 (McGuire). Case 4.

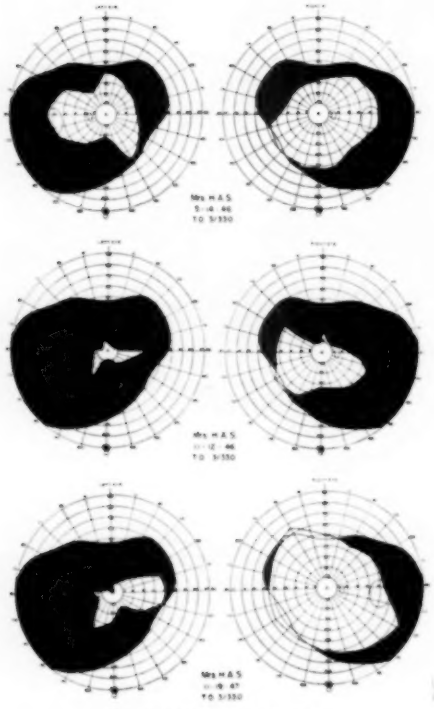
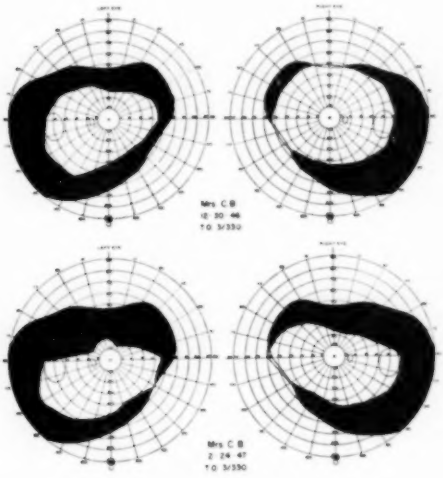


Fig. 6 (McGuire). Case 5.

the exception of the left nervehead which showed a moderate pallor and a shallow cupping.

Intraocular pressure was: O.D., 17 mm. Hg; O.S., 29 mm. Hg. The right field was full while the left showed some upper nasal contraction, although this was not marked. The patient was placed on pilocarpine but the tension remained unchanged.



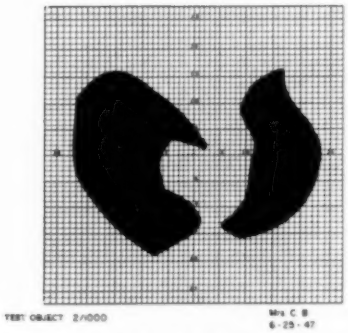


Fig. 7 (McGuire). Case 6.

On December 2, 1944, a trephination was done on the left eye. Following this procedure the tension dropped to 6 mm. Hg but, within a month, had risen to 35 mm. Hg. Miotics were again ordered and the tension was slowly reduced to normal limits.

From June, 1945, until April, 1947, the patient did not report for a checkup and, when he finally was seen on April 12, 1947, he reported that his eyes had been comfortable but that he thought he needed more help in reading. At this time the corrected vision was 20/15 in the right eye and 20/25

in the left. The fundi showed no appreciable change. Tension was: O.D., 17 mm. Hg; O.S., 22 mm. Hg.

The left field showed more contraction. On October 4, 1947, the field showed even more contraction and the blindspot a marked enlargement. Dicumarol therapy was advised. The patient entered the hospital on October 8th and received dicumarol for two weeks. On November 1st, the field showed marked improvement and, on November 29th, slightly more improvement was apparent while the blindspot had been materially reduced in size. At this time the corrected vision remained at 20/25 and the tension at 22 mm. Hg in the left eye. When last seen in April, 1948, the field and blindspot showed no appreciable change over a period of almost five months.

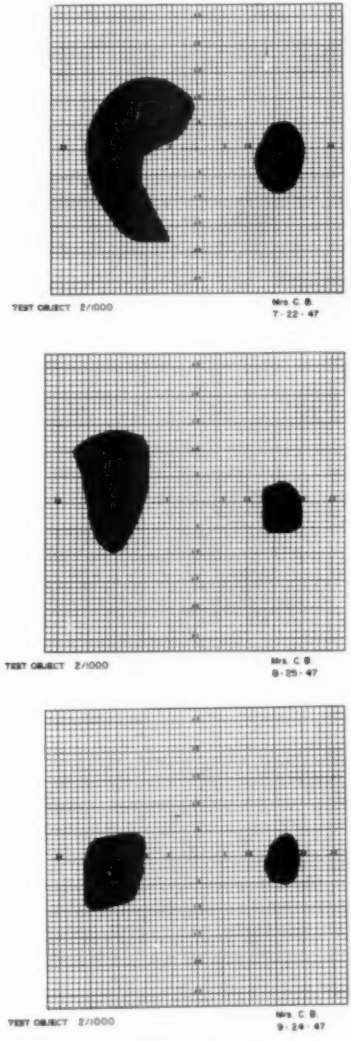


Fig. 8 (McGuire). Case 6.

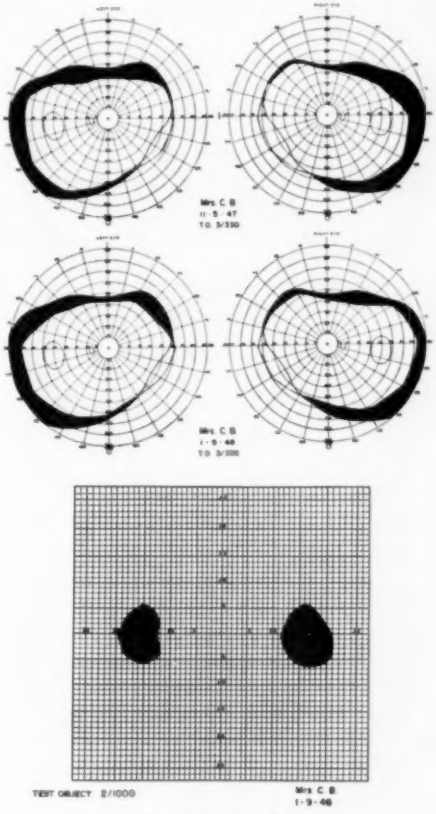


Fig. 9 (McGuire). Case 6.

Case 4. G. W. M., a white man, aged 74 years, was first seen in April, 1944, with a vision of 20/200 in each eye, corrected to: O.D., 20/70; O.S., 20/20—. There was a nuclear sclerosis in each lens and a shallow cupping of each disc.

Intraocular pressure was: O.D., 29 mm. Hg; O.S., 40 mm. Hg, and there was a slight concentric contraction of the visual field in each eye. The patient was ordered to use miotics and was followed in the office at intervals. By April, 1947, the tension had risen to 40 mm. Hg in each eye and the fields showed more cut in each eye.

In May, 1947, a flap sclerotomy was done bilaterally and dicumarol was administered for two weeks. Following operation the tension has re-

mained within normal limits and in October, 1947, the field showed marked improvement. At the last visit, October, 1947, the nuclear sclerosis had increased markedly and the best corrected vision was 20/100 in each eye.

In spite of being advised to return for periodic checkups, this patient, who lives at a considerable distance, has not returned and I have, unfortunately, lost contact with him.

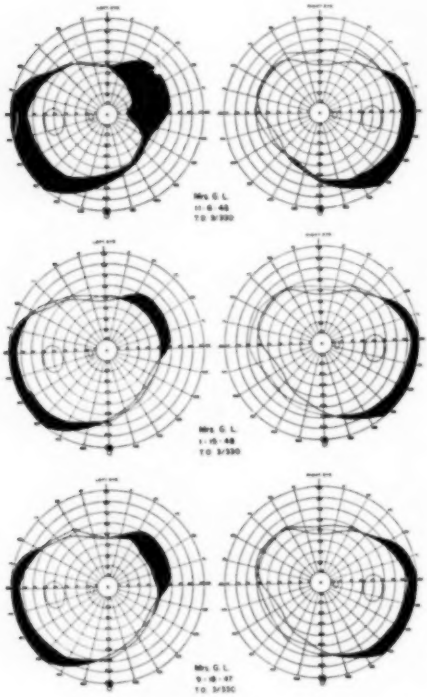


Fig. 10 (McGuire). Case 7.

Case 5. Mrs. H. A. S., aged 67 years, white, was first seen in June, 1945, when she stated that she thought she needed a change of glasses. Upon questioning she stated that for several years she had noticed that she could not see objects to the side of her direct line of vision but that she had paid no attention to this phenomenon.

Vision in the right eye was 20/50—, corrected to 20/20; in the left, 20/70—, corrected to 20/40—. The media were clear and the fundi revealed a Grade-2 retinal arteriolar sclerosis and a marked cupping of the glaucomatous type in each nerve, associated with an extreme pallor. Both visual fields showed a great deal of constriction, the left being more marked than the right. Tension was: O.D., 25 mm. Hg; O.S., 35 mm. Hg. Pilocarpine (2 percent) was prescribed four times daily.

There was no appreciable change in conditions until March, 1940, when the patient was hospitalized for a 24-hour tension curve. During this period and, in spite of the continuance of pilocarpine as before, the tension was found to be elevated in the early

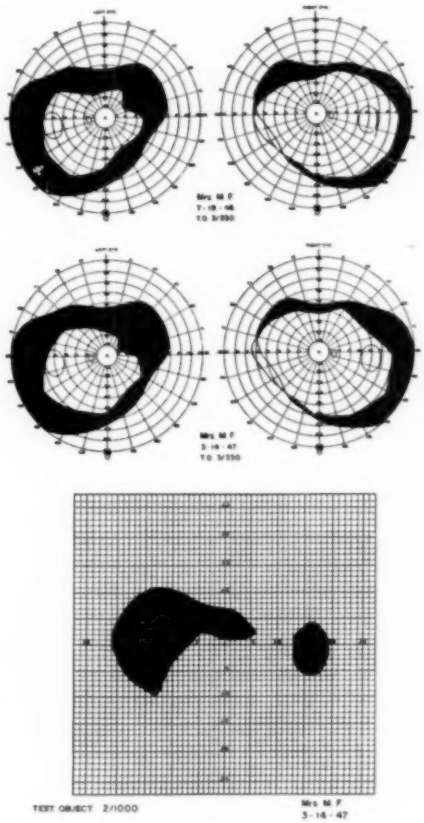


Fig. 11 (McGuire). Case 8.

morning hours to: O.D., 35 mm. Hg; O.S., 48 mm. Hg. Iridencleisis was performed on each eye with an interval of one week between operations. Immediately after operation the tension was reduced to O.D., 19 mm. Hg; O.S., 11 mm. Hg and, since operation, has never been found above 22 mm. Hg in either eye.

While the patient was still convalescent it was noted that the vascularity in each nervehead was improving, so much so in the left eye that the vessels on the left disc looked like a Medusa head of capillaries, and the color of the discs in general was much improved. When the fields were checked in May, 1946, two months after operation, they were found to be much improved, but by November 12th

of the same year they had again begun to contract. They remained in about the same stage until August, 1947, when the patient entered the hospital for dicumarol therapy which she had for two weeks.

On November 19, 1947, the right field had improved very strikingly while the left showed marked contraction with a central defect. At this time the corrected vision in the right eye was 20/20—, and in the left, 20/60 eccentric.

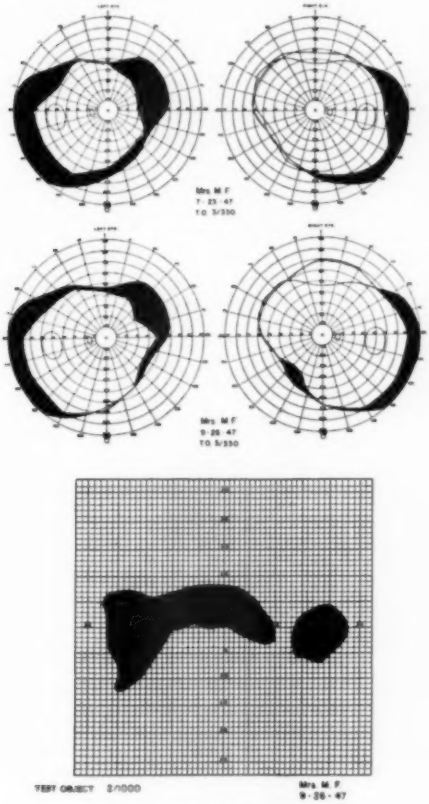


Fig. 12 (McGuire). Case 8.

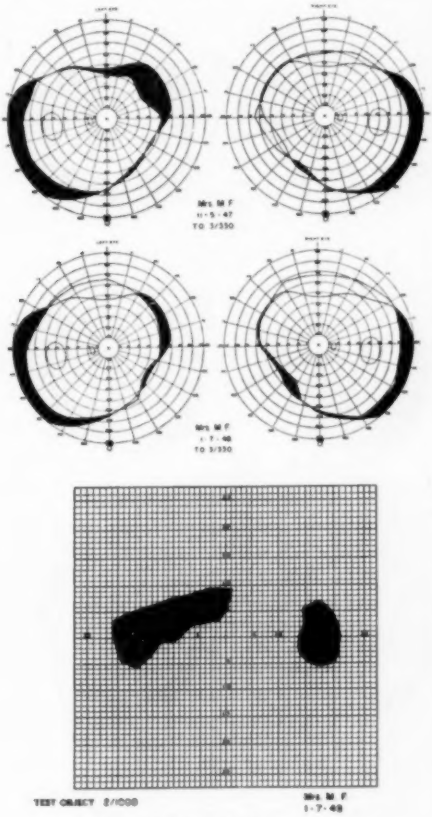


Fig. 13 (McGuire). Case 8.

June, 1946, a bilateral iridencleisis was done. Since operation, the tension has remained within normal limits but, by February, 1947, the fields showed more contraction, particularly in the upper portion, while by June 25th of that year, the blindspots had markedly increased in size.

The patient was placed on dicumarol for two weeks and one month later the central fields had improved to some extent. On August 25, September 24, November 5, 1947, and January 9, 1948, a progressive improvement was noted in both the peripheral and central fields. The corrected central vision in each eye has steadily become worse due to the development of lenticular opacities. This patient was last seen in April, 1948, when it was found that the fields and blindspots were virtually unchanged in the 3-month period.

Case 6. Mrs. C. B., aged 73 years, white, was first seen in January, 1946, with a corrected vision of 20/20 in each eye. Tension was: O.D., 26 mm. Hg; O.S., 22 mm. Hg. There was a faint nuclear sclerosis in each lens and a shallow cupping with some pallor of each disc. The fields showed some slight bitemporal contraction and there was some enlargement of the blindspots. Roentgen examination of the skull was negative with the exception of calcified posterior clinoid ligaments.

In spite of the use of miotics the tension varied between 22 and 30 mm. Hg in each eye and in

Case 7. Mrs. G. L., aged 47 years, a white housewife, first presented herself on September 4, 1947, stating that she did not think she saw well enough

with the glasses that she was wearing. She had had them for several years. Her husband was a photographer and she had made a practice of helping with work in the developing room. She had noticed that recently, after working in the darkroom for several hourse, she would have a headache and pain in the eyes.

Vision in the right eye was 20/30—, and in the left, 20/40—, each correctible to 20/15—. The media

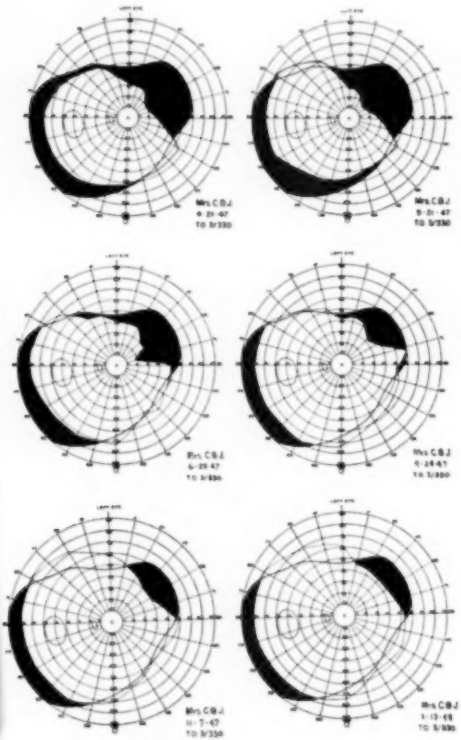


Fig. 14 (McGuire). Case 9.

were clear. The fundi were normal with the exception of the left disc which showed a very shallow cupping with a questionable pallor. Intraocular pressure was: O.D., 22 mm. Hg; and O.S., 26 mm. Hg.

Visual fields showed an upper nasal cut in the left eye and a slight concentric contraction temporally in both eyes with a beginning enlargement of the blindspot in the left eye. Two-percent pilocarpine was prescribed for each eye four times daily and, when the patient was next seen in early November, the tension was O.D., 19 mm. Hg; O.S., 22 mm. Hg. There was no change in the fields and the patient still complained of the same symptoms following work in the darkroom.

An iridencleisis was performed on the left eye on November 19, 1946, and on the right eye the following week. The postoperative course was uneventful and, upon repeated checks since operation, the tension in either eye has not varied from a low of 15 to a high of 19 mm. Hg. There was no

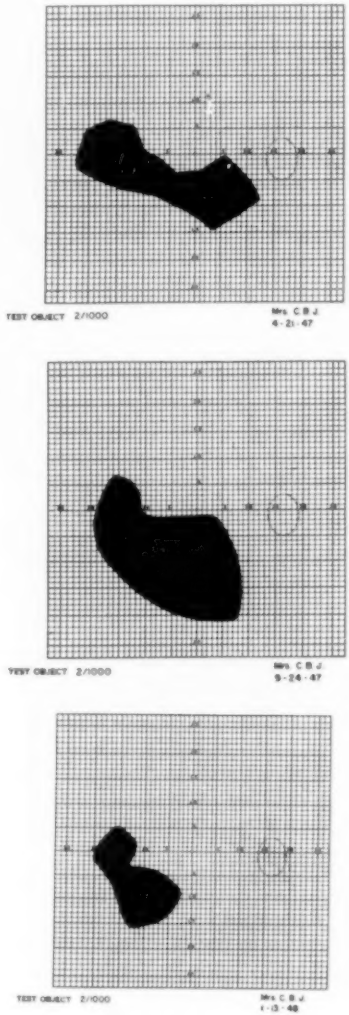


Fig. 15 (McGuire). Case 9.

material change in the fields through June, 1947, but at this time the best corrected vision had decreased to: O.D., 20/20; O.S., 20/25—.

Two months later, on August 23, 1947, the fields were unchanged from the preoperative appearance

but the left blindspot had enlarged slightly while the right was a little larger than normal.

Dicumarol therapy was advised and during the first two weeks in September the patient was in the hospital for a course of the drug. On September 18, 1947, the field and blindspots showed some improvement, while on January 15, 1948, the blindspots were normal in size and the only remaining peripheral field defect was a slight concentric contraction in the upper nasal quadrant of the left eye. At this time the corrected vision in each eye was 20/15—.

Case 8. Mrs. M. F., aged 52 years, white, was first seen in the office in June, 1945, at which time she complained of gradual loss of vision in the left eye. Vision in the right eye was 20/100 corrected to 20/15, while that in the left eye was 20/70—, unimproved. Tension was 19 mm. Hg in the right eye and 35 mm. Hg in the left eye. Nothing remarkable was noted in the examination other than a rather marked cupping and pallor of the left disc with some loss of field and a large Bjerrum scotoma above in the left eye. The patient was placed on miotics and the tension was found to be: O.D., 19 mm. Hg; O.S., 22 mm. Hg, when she was next seen several weeks later.

One year later, in spite of maintaining normal tension at every office visit the field showed more cut, while in March, 1947, there was an even greater defect in the field. At this time a flap sclerotomy was performed on the left eye and the patient was given dicumarol for two weeks. Following this the field improved somewhat but the tension in the left eye rose to 30 mm. Hg and remained at that level in spite of the continued use of miotics, also the blindspot increased in size. Consequently in October, 1947, an iridencleisis was done on the left eye followed by two additional weeks on dicumarol. In November, one month after operation, the tension was 19 mm. Hg in each eye and has remained at that level since, while at the same time the field showed considerable improvement. In January, 1948, the field was almost normal in all meridians and the Bjerrum scotoma has shown some improvement but the central vision has not been improved.

Case 9. Mrs. C. B. J., aged 36 years, white, was first seen on April 21, 1947. She stated that she had been born blind in the right eye and that, while she was still an infant, it had begun to enlarge. It had been enucleated because of pain by Dr. Louis S. Greene 10 years before I had seen her. She said that Dr. Greene had prescribed drops for the left eye and had cautioned her about constant observation of it but she had not seen him for eight years and had not used the drops for six years. There had been no pain nor inflammation in the left eye. Left vision was 20/40—, unimproved by refraction; the media were clear and the fundus normal with the exception of the disc which showed a wide and deep cup with marked pallor. The cornea measured 12.5 mm. in diameter and the intraocular pressure was 52 mm. Hg. The peripheral field showed a marked upper nasal defect and the central field a large Bjerrum scotoma below.

On the following day a flap sclerotomy after the method of Cruise was done and the patient placed on dicumarol for 10 days. One month after operation the tension had been reduced to 17 mm. Hg. and has remained in that vicinity since. There was no improvement in the field a month after the surgical procedure, but on June 28th an improvement had begun. The peripheral field showed continued improvement on September 24, 1947, but the blindspot had not responded and consequently in early October she was again hospitalized for two weeks of dicumarol therapy. By November 7, 1947, the field and blindspot showed marked improvement and when last seen on January 13, 1948, no further changes were noted. The central vision has improved to 20/20—.

Comment

Until recently there has been no alarming increase in the prothrombin time of any patients undergoing treatment with dicumarol. However, there are two recent patients who have been taking the drug at home with weekly checks of the prothrombin time, after it was thought that their maintenance dosage had been adequately determined, and who have suddenly developed hematuria with all the symptoms of renal calculus.

Upon examination by a urologist, nothing of note was found except a marked increase in the prothrombin time. Because of the experience of these two patients, I feel that it probably will be safer in using the drug to have daily checks of the prothrombin time for some weeks rather than let the patient be checked weekly after a supposed stabilization of the blood level during a 1-week or 2-week period of frequent observation.

Of the 9 cases reported in this preliminary report, 6 had dicumarol with benefit some months or years after the tension had been reduced by surgery but, in spite of the reduction of tension, the field changes showed continued progression. One patient had dicumarol immediately following operation and five months later had a second course following which there was marked

improvement in the fields. The remaining 2 patients had dicumarol immediately following operation with improvement in the visual fields. Therefore, it is impossible to say whether dicumarol was the effective agent in the gain in field or that surgery played the important role. However, it has generally been assumed in the past that the field that was lost in glaucoma was not restorable by any means except in very rare instances.

There are many questions that come to mind in relation to this problem which I cannot answer at this time. This report is presented because it has seemed to offer some hope in what has formerly been an almost hopeless condition and, while the work that has been done is purely preliminary, it would seem to warrant further investigation by many more ophthalmologists.

105 North Braddock Street.

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Historical Miniature

Egyptian Ophthalmology

Concretion of the meibomian glands and white corneal scars were recognized by the Egyptians. For the latter they applied turtle brain in honey. Their use of the aqueous of pigs' eyes as a vehicle for drugs, the brain of the turtle and man, to say nothing of blood, milk, and dung points to a faith in organotherapy which has again been advocated in our time.

Hirschberg, *Graefe-Saemisch Handbuch.*

THERAPY OF SOME OCULAR INFLAMMATIONS BASED ON IMMUNOLOGIC PRINCIPLES*

F. Herbert Haessler, M.D., and Herman A. Heise,† M.D.
Milwaukee, Wisconsin

It is our purpose to call attention to the great value of bacterial antigens in the treatment of some ocular inflammations. Its successful use depends on an understanding of a process that involves two factors: antigen and antibody. The remainder of this paper —after a few introductory remarks—will exhibit the process as simply as is consistent with adequate understanding and without violence to the truth. It will also elucidate the practical application of the principles.

Abundant clinical experience has convinced us that vaccine therapy is a great help in many situations and indispensable in some. We base our belief on our clinical experience with several dozen patients in whom resistant inflammations of the conjunctiva and of the iris were successfully treated. We will not describe this clinical material. It is too small for statistical analysis and the details of the observations on an individual patient could only illustrate a principle, not give proof of its validity. We have found it so useful in some inflammations that failed to respond to therapy with drugs or antibiotics that we want to communicate our faith in its efficacy.

The successful use of vaccine therapy depends on an understanding of immunologic principles which are not new, and which are accessible in the more comprehensive textbooks of bacteriology, such as that of Topley and Wilson.

Our purpose is to select the data which are essential to an understanding of vaccine therapy. The ophthalmologist need not have at his fingers' ends a grasp of the entire subject which constitutes the full-time occupation of the immunologist. He needs only a few principles which are easily outlined. We present such an outline which, to the immunologist, may seem oversimplified, but we believe that this outline is not only a safe guide in the treatment of patients but a true description of one of the important processes of resistance to infection.

It has the same relationship to the therapy of inflammations that a road map has to travel. The road map is not a drawing of the countryside, but a series of symbols that are easily understood and if properly applied lead the traveler to his destination without danger or detours. Similarly, our scheme is a simplified diagram which is a symbol for the essential reactions that take place in the resistance to infection. It is not only a safe guide to therapy but also to an understanding of fundamental processes in infection, tuberculin therapy, and allergy.

The immunologic principles

The fundamental mechanism of the tissue injury that results from the introduction of all organisms except the few that are primarily toxic—diphtheria, tetanus, gas bacillus, and botulinus—and also from the nonliving agents in allergic individuals, is the reaction between antigen and antibody. Most antigens are protein and in infections they are protein from the protoplasm of the invading organisms. The tissues of the host react to the invasion of antigen by the production of antibody. Antibody is doubtlessly not a single simple substance but all the reactions in which it is involved can be understood by conceiving of it as a single reacting unit. In this discussion it will be referred to as a substance.

Antigen alone is harmless to all tissues. As time goes on, antibodies develop in response to its presence. Antibodies alone are also harmless but when antigen reacts with

* From the Department of Ophthalmology, Marquette University School of Medicine. Presented at the 84th annual meeting of The American Ophthalmological Society, Hot Springs, Virginia, May, 1948.

† By invitation.

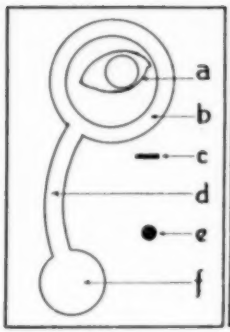

FIG. 1

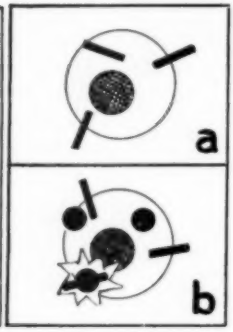

FIG. 2

Fig. 1 (Haessler and Heise). Identification of symbols in the other figures: (a) Eye. (b) Circulation of fluids in tissues in and about the eye. (c) Antigen. (d) Blood stream. (e) Antibody. (f) Skin.

Fig. 2 (Haessler and Heise). Fundamental characteristics of antigen and antibody: (a) Antigen alone is harmless to a cell. (b) Antigen combined with antibody that is attached to a cell is destructive.

antibody that is attached to a tissue cell, the reaction is destructive. It is the immunity, not the antigen, that causes the trouble. Antigen increases because of multiplication of the invading organism. Antibody increases in response to the increased antigen. When enough of both substances is present to involve many cells in a tissue, clinical signs of inflammation become manifest.

The interval of time between the first introduction of antigen and visible signs of inflammation is the incubation period of the disease. It is the proliferation of antibody, not the supposed accumulation of enough antigen to injure tissue cells that marks the end of the incubation period. This was pointed out by von Pirquet years ago and still is not clear to everyone. Antibodies may be elaborated at a much greater rate than antigen. When they are, 1 or more of 3 events will take place:

1. The antibody destroys the antigen at the site of invasion.

2. The antibody enters the body fluids. Antigen-antibody reactions that take place here—humeral reactions—are harmless to the primarily inflamed tissue.

3. The antibody may become concentrated in a secondary focus in some other tissue. When it does, this tissue will become inflamed immediately if antigen is introduced into it. This is the probable process of focal infection.

The first 2 of these 3 reactions lead to healing at the original site of inflammation but leave the tissue "sensitive" to reintroduction of the same antigen. The word "immune" may be substituted for "sensitive" in this sentence. It is identical in meaning. In the course of time, however, the supply of antibodies gradually decreases and the tissue loses its sensitivity but, if a similar antigen should be introduced anew, the production of antibodies will proceed much more rapidly.

The essential processes of acute inflammation and spontaneous recovery have just been described. However, antibody is not always developed in adequate quantities to deplete the invaded tissue of antigen. It may develop just rapidly enough to keep the antigen in check, and yet not rapidly enough to wipe it out completely. In this event a long-continued smouldering inflammation results—the situation for which vaccine therapy is indicated.

Vaccine therapy is essentially the introduction of an antigen similar to the invading one into tissues of another organ—not the infected one. In practice, this other tissue is almost always the skin and the process has unfortunately been named "desensitization." Actually we are not desensitizing the skin but rather sensitizing or immunizing it. We are inducing it to become the site of origin of an adequate supply of antibody. When treating an eye, we strive to inject antigen into the skin in such quantity that local antigen-antibody reactions will take place in the skin and humeral antigen-antibody reactions which are harmless to the eye will deplete the eye of antigen. The essential point in understanding vaccine therapy is that we are not desensitizing any tissue; on the contrary, we are sensitizing another tissue—the skin. We are shifting the site of the harmful

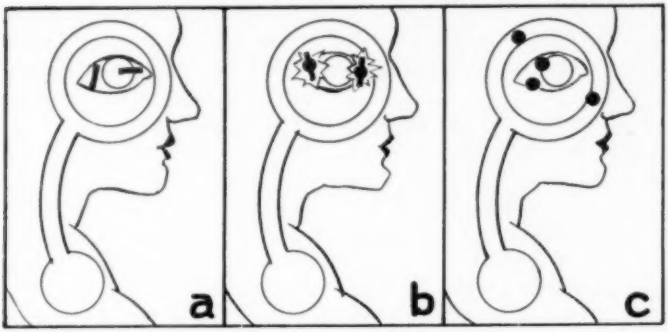

Fig. 3 (Haessler and Heise). Infection, incubation period, and spontaneous recovery: (a) Antigen alone, derived from invading organism, produces no inflammation. Antibodies gradually develop. This is the incubation period. (b) Antigen and antibody react in tissues of eye and cause inflammation. (c) Antibodies have destroyed antigen. Eye has recovered.

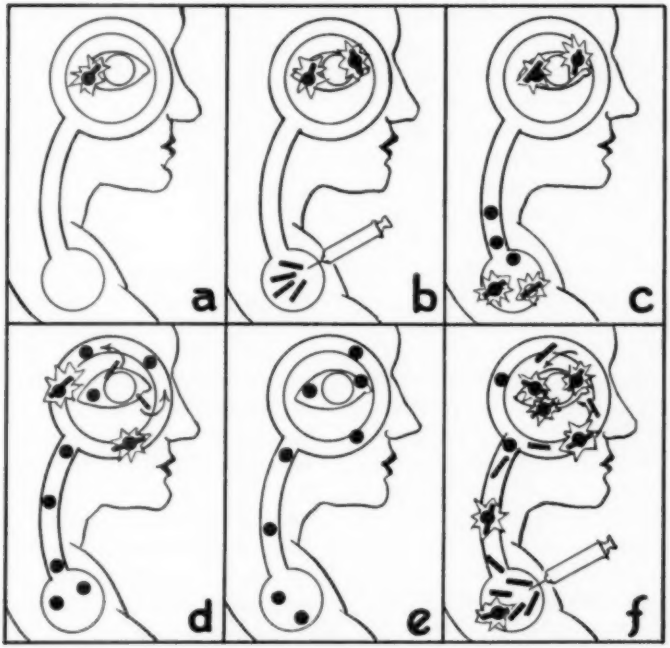

Fig. 4 (Haessler and Heise). Treatment. (a) Eye is inflamed. Antigen-antibody reactions in eye. (b) Antigen is introduced into skin. (c) Skin elaborates antibodies. Excess antibodies enter blood stream. (d) Antigen enters circulating fluids from eye. Humeral reactions destroy antigen. Eye recovers. (e) Antibodies only in skin, blood stream, and eye. No inflammation. All tissues immune; that is, sensitive to further introduction of the same antigen. (f) Overdose of vaccine. Excess antigen enters blood stream and eye, where it reacts with antibody and produces inflammation.

antigen-antibody reaction from the eye to the much less vulnerable skin. The essence of the treatment is the shifting of the shock organ.

The danger of vaccine therapy is overdosage. If we give too large a dose, we introduce a quantity of antigen that is large enough to produce a harmless local reaction in the skin, a harmless humeral reaction, and to leave an excess of antigen that will reach the eye and produce a dangerous focal reaction there. A proper dose inadvertently injected into a vein produces the same deleterious effect as an overdose.

These reactions take place with all nontoxic antigenic substances, living or dead, of whatever source. The principles of treating allergic lesions are precisely similar.

Details of vaccine therapy

The practical corollaries of the reactions are these: One must have a vaccine which contains the antigen which is the cause of the inflammation. In conjunctival inflammations a suspension of a 24-hour heat-killed culture of the invading organism is the surest and most convenient source of antigen. When the causative organism gives rise to a soluble antigen, the filtrate of a 4-day veal brain broth culture diluted to 1:10,000 is efficacious. In iritis a similar culture from the tissue of primary infection, for example, nose, throat, or prostate, is often available. If it is not, stock cultures of the common etiologic factors, usually streptococcus, pneumococcus, and staphylococcus, can be used. In probable tuberculous lesions a tuberculin or P.P.D. are readily available antigens.

The important factors to emphasize about dosage are size and interval. The dose must never be large enough to produce a focal reaction. We use extremely small doses with success. We start with the intracutaneous injection of 0.01 cc. of a suspension of organisms from a 24-hour culture (not over 10 million organisms) and gradually increase the dosage in succeeding injections until we note clinical improvement of the lesion. After that we no longer increase the dose. There is no theoretical reason for doing so and our practical experience encourages us to be guided by reasoning based on the theory we have outlined.

This is probably as true of tuberculin as of other antigens but we do not, as yet, have adequate clinical data on the basis of which we could affirm or deny this statement with confidence.

The interval between injections may be 3 to 5 days in the beginning of treatment when the dose is small. Later the interval may be increased but not to an extent that there is a falling off in the production of antibodies. The patient's observations are of use in determining this interval. Frequently we have been told by a patient who had been asked to return in 2 weeks that he felt well for 6 days and then gradually became vaguely uncomfortable.

The illustrations in the text represent crucial moments in the diagrammatic motion picture that accompanied the presentation of this essay.

Summary

When the tissue of a host is invaded by antigen, it responds with the development of antibody. Neither the antigen nor the antibody is harmful to the tissue. The reaction of antigen with antibody that is attached to a tissue cell is destructive to the cell. If the number of antibodies exceeds the antigen, spontaneous healing takes place. When it does not, one strives in rational therapy to have this antigen-antibody reaction take place in the body fluids or in a less vulnerable organ, the skin. Injection of antigen into skin in minute quantities accomplishes this object without danger. An excessive injection is dangerous because the excess of antigen can reach the diseased organ and increase the inflammatory process.

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SCLERAL STAPHYLOMA AND RETINAL DETACHMENT*

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In 1940, before this society, I reported a case of equatorial scleral staphyloma and retinal detachment successfully cured by excision of the staphyloma. In 1945, the second eye of this patient developed scleral staphyloma and retinal detachment. The staphyloma was excised and the retina became reattached. The latest report from this patient indicated that she had no further disturbance in either eye and the corrected vision has remained useful (20/30+ in the right eye, 20/40+ in the left).

Since then, in a recent series of 34 retinal detachment cases, 8 additional cases, all more or less similar, of scleral staphyloma and retinal detachment have been operated upon by me. The series is too small to draw any conclusions regarding the frequency of this finding, but is significant in indicating that the combination of staphyloma and detached retina is perhaps not infrequent.

So far as could be determined no other author, surprisingly enough, has reported this association. It is incredible, when one considers the enormous amount of time and work devoted in the past to studies of the pathogenesis and pathology of retinal separation, that this circumstance was not encountered and remarked. It is therefore entirely possible that somewhere in the vast literature on retinal detachment, a note of this combination and its significance is to be found.

PATHOGENESIS

The pathogenesis of scleral staphyloma has had little study and attention. Considered as a part of the terminal stage in absolute glaucoma or the result of obvious injury or inflammation of the sclera plus increased intraocular pressure, it has been lightly dismissed in our systems of ophthalmology and textbooks, except in that of Fuchs's. Mention is made of the three types, classified for many years as intercalary, ciliary, and equatorial staphylomas, depending on their location.

Birnbacher and Czermak, in 1886, were the first authors to discuss the evolution and progression of scleral staphyloma. According to Mattice, from whom I have freely borrowed, these authors assumed that a weakened spot in the sclera begins to yield before a normal or increased intraocular pressure. Since the sclera is relatively inelastic, the inner fibers cannot stretch sufficiently to preserve their integrity, and finally break off short, the broken ends retracting somewhat. Successive layers of scleral fibers are thus exposed to the disintegrating process and are broken through. The scleral wall becomes thinner and yields altogether to the force of the intraocular pressure, thus forming an ectasia.

The histologic findings of these authors revealed that the edges of the excavation on the inner surface of a large and old staphyloma are slanting and that it presents a roughened surface due to the irregularly broken ends of the scleral fibers. Only the deepest (that is most superficial) fibers that form the floor of the excavation are intact. These fibers, however, may later rupture until eventually the scleral wall is broken entirely through.

The relation which the uvea bears to such staphylomas was found to depend upon the degree of inflammation in the sclera and uvea. In cases where very little inflammation has occurred, the uvea retains its normal position and bridges across the mouth of the excavation. However, in cases with more extensive inflammatory changes and exudation, the uvea is found firmly attached to

* From the Department of Opthalmology, Northwestern Medical School. Presented at the 84th annual meeting of the American Ophthalmological Society, Hot Springs, Virginia, May, 1948.

Fig. 1 (Vail). Scleral staphyloma, showing the torn fibers of its inner third.

the sclera as a thin atrophic layer lining the walls and floor of the excavation.

If scar tissue has been found in the uvea prior to the beginning of the staphyloma, the uvea is found ruptured since stretching is impossible. A normal uvea, however, may also rupture if the mouth of the excavation becomes too wide. In most of their cases, Birnbacher and Czermak found the choroid adherent to the walls and floor of the excavation. As a result of their studies, these authors laid down two general rules which govern the formation of staphylomas:

1. Inflammatory changes can always be demonstrated in the sclera.

2. The staphyloma always develops at a point of least resistance in the sclera, for example, where it is perforated by blood vessels.

Mattice, in 1913, described the histologic findings in a case of equatorial staphyloma that had no connection whatever with the point of entrance of blood vessels, nor with inflammatory changes that could be observed in either retina, choroid, or sclera. The choroid was not pressed against the floor of the excavation but loosely filled out the space between the floor and the lamina vitrea, bridging over the mouth of the excavation, indicating that intraocular pressure alone was not responsible for the ectasia. The floor of the excavation was covered by a ciliary artery and nerve and Mattice thought that this relationship had a direct bearing on the origin of the excavation. He compared this finding to the gradual grooving of bone by arteries with age and considered that the continued action of blood pressure within the walls of the ciliary artery, particularly if sclerotic or calcified, would form a groove in the sclera, especially if the latter were weakened by disease or injury.

Fuchs mentioned the diminished resistance of the sclera as an infrequent cause of ectasia of the sclera even in the presence of normal intraocular pressure. It is found in cases of deep scleritis, tumors (malignant neoplasms, gummatous or tuberculous nodules), and injuries, especially ruptures of the sclera. He said, "Scleral ectasiae arising in this way lead subsequently to elevation of the intraocular pressure, which then, however, must be regarded not as the cause, but as the result of ectasiae, even though, just as in the case of ectasiae of the cornea, it does contribute to make the latter larger still."

A study of two specimens of scleral staphyloma found in the pathologic laboratory of the Eye Department, Northwestern University, brings out several very interesting points in support of the work of Birnbacher and Czermak.

Figure 1 is an illustration of a section of an eye removed from a patient, aged 77 years, for a suspicious intraocular tumor and secondary glaucoma. The histologic diagnosis in addition to the staphyloma was an occlusion of the central vein. A staphyloma the size of a globe, with smooth surface, was found beneath the internal rectus muscle, measuring 25 by 21.5 by 22 mm.

There is marked thinning of the nasal sclera from the ora serrata backward to

well beyond the equator. Just in front of the equator there is a circumscribed scleral staphyloma within which the inner third of the scleral fibers are torn, while the outer two thirds bulge sharply outward. Between the frayed ends of the torn fibers, filling the staphyloma, there is a loose areolar tissue which contains a few round cells and many fibroblasts. The choroid and retina in this and the immediately adjoining region are reduced to a thin, partly fibrous, partly glial membrane, which does not follow the outline of the staphyloma but crosses or bridges it. Anterior to this region the retina shows excessive cystoid degeneration. The nasal sclera in general shows poor stain of its nuclei. Several small, thin-walled vessels course through the staphylomatous portion of the sclera. There is marked retinal and choroidal vascular sclerosis throughout.

The second specimen is that from a patient, aged 75 years, (fig. 2). No history is obtainable. The histologic diagnosis is secondary glaucoma. The globe measures 30 by 24 by 24 mm. (high myopia). There is a circumscribed staphyloma in the diffusely thinning sclera of the posterior polar region. The inner two thirds of the scleral fibers are torn, leaving frayed edges, the outer third bulges in an ampulliform fashion. Its inner surface is lined by extremely atrophic choroid and the thin outer wall of a large retinal cyst. There is a detachment of the posterior vitreous. The subhyaloid region and the retinal cysts are filled with the same pink coagulum. Anterior to the staphyloma is to be found an enormous area of cystic degeneration of the retina. The outer wall has prolapsed into the scleral staphyloma.

Fig. 2 (Vail). Scleral staphyloma, showing ruptured scleral fibers and containing a retinal cyst.

Fig. 3 (Vail). Adjacent to the staphyloma which shows a cystic degeneration of the retina with bands of glial fibrous strands across the cyst.

These two specimens are, I believe pertinent to the discussion since they reveal the method of the development of the staphyloma of the sclera supporting the previous histologic studies of this condition by other authors and also indicate that even in the presence of increased intraocular pressure, the retina may bridge over the staphylomatous area. In addition, Figure 3 reveals the mechanics of the development of a retinal

tear as a result of contraction of glial fibrous bands in a retinal cyst.

We see, therefore, that a staphyloma of the sclera can arise in different ways. Scleritis and episcleritis are not unusual ocular diseases. Other factors besides inflammation of the sclera may play a role in weakening its inner wall, factors such as choroiditis, cyclitis, endarteritis, phlebitis, or perhaps some nutritional condition of the sclera comparable to scleromalacia or senile hyaline scleral plaques.

It is easy to conceive of the development of a tear in the inelastic retina bridging over a diseased area in the sclera that is stretching and yielding to intraocular pressure. This is particularly likely when one considers that the retina in this area is probably diseased and cystic as is seen histologically. Such a tear was found in almost all of the cases about to be described.

Case reports

Case 1. A woman, aged 57 years, had a large balloon detachment of the retina in the upper temporal portion of the left eye. No tear was observed. The ocular tension was subnormal; transillumination was negative for shadow. On exposure of the scleral operative field, a scleral staphyloma occupying the area between the tendons of the superior and external rectus muscles was found. It measured 12 by 16 mm. and began abruptly at a point 6 or 7 mm. from the limbus. The staphyloma was excised more or less according to Müller's technique. A cure of the retinal detachment resulted and the patient has retained useful vision in the left eye since then. (Case reported in 1940.)

Case 2. The same patient described in Case 1. In 1945, she developed a similar detachment in the upper temporal portion of the right eye. No tear was seen and the ocular tension was subnormal. A staphyloma of the sclera in the area of the detachment was observed. On exposure it was found to arise abruptly about 10 mm. from the limbus and measured approximately 20 by 7 mm., between the 8- and 10-o'clock positions. This was excised in a fashion similar to the operation done on her left eye. A cure of the detachment resulted and the vision in this eye has likewise remained good to date. (Case reported in 1946.) The refraction changed as the result of the operation from, R.E., −0.5D. sph. ⊃ −0.75D. cyl. ax. 175° to +1.25D. sph. ⊃ +4.5D. cyl. ax. 175°; L.E., from −1.0D. sph. ⊃ +1.75D. cyl. ax. 115° to +3.5D. sph. ⊃ +3.25D. cyl. ax. 25°.

Case 3. A man, aged 60 years, was examined on November 11, 1946. Four weeks before he noticed a veil descending over the vision of the left eye. A large dark balloon detachment of the retina was found in the upper temporal portion. A very large horseshoe-shaped tear was observed 18 mm. from the limbus at the 1-o'clock position. Ocular tension was subnormal (14 mm. Hg, Schiøtz). Transillumination was negative.

At operation on November 23, 1946, an irregularly shaped staphyloma of the sclera was found. It measured 8 by 10 mm. and arose abruptly 10 mm. from the limbus. There was some question for a moment if this could be a melanoma of the choroid. However, light shone through it readily and the sclera was obviously thinned and dented easily on palpation with the tip of a muscle hook. Instead of excision, a series of ignipunctures in and around the area was performed and some yellowish subretinal fluid was evacuated. On the tenth postoperative day a massive vitreous hemorrhage occurred which began to clear shortly before his discharge from the hospital on December 14, 1946.

On his return three weeks later, the retina at the site of the operation was found to be in place and showed the usual postoperative pigment action. However, in the floor the retina was detached in a trilobular fashion. On February 1, 1947, the involved area was operated on with diathermy coagulation, without a completely successful reapposition of the retina. Final vision on May 21, 1947, was counting fingers at 10 feet. Tension was 22 mm. Hg (Schiøtz).

Case 4. A woman, aged 59 years, was examined on March 12, 1947. Five days before she had noticed blurred vision in the left eye. An extensive detachment of the retina in the temporal area of the left eye from the 2- to 7-o'clock positions was seen. The retina was in folds with the area of greatest detachment at the 4-o'clock position. No tears were seen and transillumination was negative for shadows. The ocular tension was subnormal.

At operation, a staphyloma of the sclera arising 9 mm. from the limbus and measuring 8 by 6 mm. at the 3-o'clock position was seen. It was excised according to the modified Müller technique. Nonperforating ignipunctures were made on each side of the scleral excision. The result was a failure. The retina remained detached from the 4- to 8-o'clock positions.

Case 5. A man, aged 46 years, was examined on April 2, 1947. He had a detachment of the retina in the right eye of two weeks' duration. A balloon, dark detachment was seen beginning at the 10-o'clock position and extending to 3 o'clock. There was a large horseshoe-shaped tear at the 12-o'clock position and 16 mm. from the limbus. Another fishhook vertical tear, not connecting with the first one, at the 1-o'clock position, extended to 18 mm. from the limbus. The ocular tension was low, 10 mm. Hg (Schiøtz).

At operation, a large staphyloma of the sclera extending from the 10- to 1-o'clock positions, arising 10 mm. from the limbus and extending to the equator, was found. The area was extensively treated

with diathermy ignipunctures, most of which were perforating, and particularly heavy in the area of all tears. The sclera shriveled under the treatment. At the first dressing, 48 hours later, the interior of the eye was found filled with blood and there was a severe ocular reaction. The blood gradually absorbed, but traces of it were still present three months later, and the posterior surface of the lens above was blood-stained. This has persisted.

The retina was reattached and the field of vision became full. Ocular tension on September 27, 1947, was 16 mm. Hg (Schiøtz). Preoperative refraction was: −0.5D. sph. ⊃ −2.5D. cyl. ax. 90° (vision, 20/20. Postoperative refraction on September 27, 1947, was: −0.5D. sph. ⊃ 3.0D. cyl. ax. 110° (vision, 20/30.)

As a result of the extensive diathermy of the sclera beneath the superior rectus tendon, severe scarring resulted and there remained 25 degrees exotropia and 14 degrees right hypertopia in the primary position, necessitating later freeing of the adhesions and recession of the external and superior rectus tendons with considerable improvement, but still marked limitation of movement downward and outward. An annoying diplopia is therefore still present, although the patient is learning to suppress the vision in the right eye.

Case 6. A man, aged 22 years, was examined on April 18, 1947. The upper temple part of the retina in the left eye had become detached in 1941 and was operated upon successfully with diathermy coagulation. No staphyloma of the sclera in that eye was noted. In October, 1946, the patient noticed blurring of vision in his right eye. Examination on April 18, 1947, showed what was considered to be a large cystic detachment of the retina involving the temporal zone from the 5- to 11-o'clock positions with multiple small tears in a disinsertion zone at 9 o'clock particularly. Tension was 15 mm. Hg (Schiøtz).

At operation on April 21, 1947, a bluish rectangular staphyloma of the sclera was observed beneath the tendon of the lateral rectus muscle and extending about equally above and below the edges of the tendon. It measured 12 by 20 mm. and began about 8 mm. from the limbus. A scleral resection of the staphyloma, 10 by 16 mm., was performed and the area around the wound was treated with perforating ignipunctures. The retina did not become reattached and the result was a failure. Postoperative tension was 12 mm. Hg (Schiøtz).

Case 7. A woman, aged 43 years, was examined on April 18, 1947. The left eye had had a retinal detachment seven years before and was operated on elsewhere with failure. A funnel-shaped detachment was now present. About March 15, 1947, she noticed blurred vision in the right eye. A large balloon detachment of the retina was found in the temporal portion of the right eye, extending from the 7- to 11-o'clock positions. It was of dark color and encroached onto the macular area. At the 8-o'clock position could be seen a series of small round holes in the cystic (shagreen) retina, 16 to 18 mm. from the limbus. Tension was 12 mm. Hg (Schiøtz).

At operation a bluish discoloration was noticed beneath the tendon of the lateral rectus. It measured 12 by 12 mm. and was roughly triangular in shape. It dented easily on pressure and transilluminat.on of the area revealed a thin sclera. A 12 by 8 mm. strip of sclera was excised. The underlying choroid was present and not adherent to the sclera. It was obviously atrophic. A small amount of vitreous was lost. The lips of the wound were treated with diathermy coagulation (nonperforating) after the sutures were tied. A successful result ensued. Preoperative refraction was: −1.5D. sph. ⊃ 1.0D. cyl. ax. 35° (vision, 20/100). Postoperative refraction was: −1.5D. cyl. ax. 60° (vision, 20/40+).

Case 8. A man, aged 76 years, was examined on December 12, 1947. His right eye had been lost as the result of an accident at the age of 21 years. An extracapsular cataract extraction was done in the left eye on July 27, 1946, followed at intervals by two needlings and a capsulotomy (October 26, 1947). On November 11, 1947, his vision became blurred and a detachment of the retina developed in the temple side of the eye.

At operation a staphyloma of the sclera was observed. It resembled a leaf, the inferior portion lying largely under the lateral rectus muscle, measuring 9 by 8 mm., and a superior portion extending vertically and laterally, measuring 4 by 6 mm. There was a connecting isthmus between the two leaves. A piece of sclera from the 2- to 4-o'clock positions, 5 mm. wide and 12 mm. from the limbus, running through as much of the staphyloma as possible, was excised. No diathermy was used. A considerable amount of fluid vitreous escaped, and the eye became very soft. Failure resulted.

Case 9. A woman, aged 62 years, was examined on January 30, 1948. Two months before she had noticed sudden partial loss of vision in the left eye, and three days after onset she awakened to find the sight in the left eye "gone." Examination on January 30, 1948, revealed an extensive detachment of the lateral part of the retina of the left eye from the 11- to 5-o'clock positions, with the area of greatest elevation at 2 o'clock. Here could be seen a large horseshoe-shaped tear 18 mm. from the limbus. The retina was dark in color. Tension was 10 mm. Hg (Schiøtz) and transillumination was negative for shadows. There was an incipient cataract present in each eye.

At operation a staphyloma of the sclera was discovered. It was situated between the tendons of the superior and lateral rectus muscles. It consisted of three radial bluish pigmented areas about 1 to 2 mm. wide, each one beginning at 8 mm. from the limbus. The entire area involved was approximately 8 mm. wide and extended just beneath the upper edge of the lateral rectus tendon.

An elliptical area, 14 by 5 mm., of the sclera, 8 mm. concentric to the limbus, was outlined with a knife. Four double-armed (cutting-edge needles) 4-0 black silk sutures were placed in mattress fashion from sound sclera to sound sclera and tightly tied. There resulted a tuck of the staphyloma. Loss of subretinal fluid occurred around the

sutures, softening the eyeball, and thus increasing the ease of tying them. The tucked portion of the staphyloma was excised, and several gaps were closed with single black silk sutures. About 25 diathermy punctures were placed around the wound. Healing was uneventful in spite of the difficulty of keeping this patient quiet.

Preoperative refraction was: +1.0D. sph. ⊂ −2.0D. cyl. ax. 45° (vision, light perception). Postoperative refraction (April 1, 1948) was: +0.5D. sph. ⊂ +1.75D. cyl. ax. 120° (vision, 20/50). The postoperative field was full; there were some vitreous opacities and the tension was 16 mm. Hg (Schiøtz).

Case 10. A man, aged 59 years, was examined on February 10, 1948. One week before, the vision in his left eye suddenly blurred. Examination of the left eye showed some lens spicules, a few floating opacities and a large balloon-shaped retinal detachment extending from the 11- to 5-o'clock positions as far as the optic nervehead. The outline was sharply defined. There was a large horseshoe-shaped tear at the 2-o'clock position, 16 mm. from the limbus and a second round tear at 3 o'clock, 19 mm. from the limbus. The color of the detachment was dark. Transillumination revealed no shadow. The ocular tension was 14 mm. Hg (Schiøtz).

At operation (February 18, 1948) a staphyloma of the sclera was found extending from the 12- to 5-o'clock positions. The posterior border was 18 mm. from the limbus and the staphyloma measured 11 mm. by 30 mm. It arose about 7 mm. from the limbus. There were radial lines and areas in the staphyloma, reflecting the bluish color of the choroid. It was darkest at the 2-o'clock position and lightest at 10 o'clock.

Four mattress sutures of 4-0 silk were inserted in the staphyloma from 12 to 17 mm. from the limbus from 1 to 4 o'clock. A tucking of the sclera was therefore made and a piece of sclera, roughly 5 by 11 mm., was excised. The closure of the wound was further secured by placing of several single-armed silk sutures in gaping areas. A large amount of fluid vitreous, and a bead of solid vitreous was lost.

A row of perforating ignipunctures was made with the diathermy, 12 and 18 mm. from the limbus from the 12- to 5-o'clock positions. Another series of nonperforating diathermy punctures was made on either side of the scleral wound. The conjunctiva was closed with continuous black silk sutures. Inspection of the retina at the close of the operation revealed many folds in the area of the resection. The media was clear.

There was considerable postoperative reaction, as manifested by edema and chemosis of the lids and bulbar conjunctiva. For three weeks there was no red reflex obtainable; the retina in places could be seen with oblique illumination. Although the patient had good light perception, the prognosis was considered hopeless. At the end of three weeks the edema and chemosis had cleared and a red reflex became apparent, first on the nasal and later on the temple side.

On April 22, 1948 (two months after the operation), the ocular congestion was clearing. The peripheral field of vision was full except for a small notch up and out. There was a small central scotoma. The red reflex was bright. A large scar of the retina, with pigmented edge, occupied the temple portion of the eyeball, with some blood-staining of the retina in the floor extending into the macular area. The tension was 12 mm. Hg (Schiøtz).

Preoperative refraction was: +1.5D. cyl. ax. 75° (fingers at 10 feet). The postoperative refraction two months later was: −1.0D. sph. ⊂ +4.5D. cyl. ax. 180° (20/100+).

Comment

Two of the described cases were treated with diathermy alone. One was a failure. The successful one, however, had had so much coagulation, some of it involving the ciliary zone, that a severe intraocular hemorrhage and cyclitis resulted, leading to a long convalescence and resultant and perhaps permanent blood-staining of the posterior surface of the lens and vitreous. In addition, so much scar tissue bound down the superior rectus muscle, and to some extent the external rectus muscle, that a marked muscle imbalance occurred, requiring further surgery in an effort to overcome a very annoying diplopia.

The rest of the patients were operated upon by scleral resection combined with some diathermy coagulation. The last two patients were treated surgically by mattress sutures passed through the staphyloma which, on being tied, resulted in a tuck of the sclera that was then excised without too much difficulty. This idea was obtained from Gayer Morgan who, in 1943, successfully excised a ciliary staphyloma in this fashion. It is apparently safer and easier to perform than is the more tedious excision hitherto described by Müller, Lindner, Pischel, and myself.

The placing of a row of perforating ignipunctures near to the wound further enhances the chances of success and the avoidance of hemorrhage. Of the 8 cases of scleral resection, 4 were total failures; 3 can be considered successful and 1 a partial success. The operations were all performed under sodium pentothal intravenous anesthesia, and the usual method of exposure of the field of operation was performed.

Conclusions

This small series of cases permits one to draw the following conclusions:

1. Retinal detachment may occur subsequent to a scleral staphyloma in the affected area.

2. In most of the cases the detachment was dark and ballooned. There was usually to be found a large horseshoe-shaped tear in the area of greatest detachment.

3. Most of the staphylomas occurred in the lateral portion of the eyeball.

4. Unless the staphyloma is small, diathermy alone offers the least chance of successful surgery.

5. Excision of the staphyloma, after first tucking the affected sclera, appears to be relatively simple to perform. Diathermy ignipunctures can be placed around the scleral wound, thus increasing the chance of success and reducing the hazard of intraocular hemorrhage.

6. Scleral staphyloma and retinal detachment occur perhaps more frequently than has hitherto been realized, and the presence of a staphyloma is more common than suspected.

7. The diagnosis is made by the bluish, bulging appearance of the affected sclera, the easy indentation of its surface, and its increased transparency on transillumination.

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THE USE OF PROCAINE INTRAVENOUSLY IN OPHTHALMOLOGY*

A preliminary report

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The recent introduction of intravenous procaine infusion in the management of pain in trauma and inflammatory conditions, as well as in the pruritus of jaundice, the treatment of burns, as a substitute for morphine in postoperative care, and for serum sickness, has suggested the need for an investigation as to its possible value in ocular disorders.

In reviewing the literature on the use of intravenous novocaine in ocular disorders, the following are worth recording:

Lutton, Roumer, Giroud, and Ferron were able to combat eclamptic amaurosis by the intravenous administration of recorcoin. Esente[1] used it in painful glaucomas where the results mostly were satisfactory (no statistics). Pain was relieved and intraocular pressure was reduced for much longer than the time during which the drug was administered. He noted that the simultaneous use of miotics may enhance these effects. The doses

* From the Service of Dr. Raymond Meek, New York Eye and Ear Infirmary.

given varied between 10 and 100 centigrams.

Mme. S. Schiff-Wertheimer and Mlle. Gaillard[2] used intravenous novocaine (1:100) in the treatment of thrombosis of the retinal veins. Uncertain results were had in central retinal-vein occlusion but satisfactory results were had in branch obstructions if they were treated early enough.

Lorofi[3] used intravenous novocaine in the treatment of visual difficulties caused by arsenical trypanocides. He had only 2 failures, with 7 successes and 2 ameliorations. When blindness was complete, 3 cases were successful and 2 were improved of the 7 cases observed.

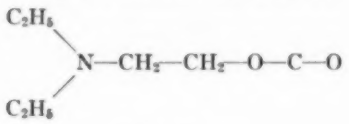
Rouher[4] used intravenous novocaine in the treatment of retinal edema and found quicker absorption and lessening of visual disturbances that could be attributed to the injections.

Chemistry

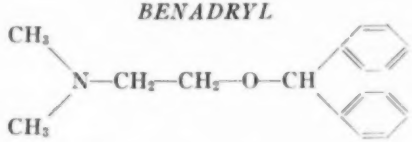
Procaine is para-aminobenzoldiethylaminoethanol, soluble in one part of water in which its reaction is neutral. It is stable and does not decompose at temperatures as high as 100°C. When injected intravenously in sublethal doses, two processes are initiated: (1) Hydrolyzation of procaine by an enzyme into para-aminobenzoic acid (PABA) and diethylaminoethanol (DEA); (2) acetylation of para-aminobenzoic acid.

Nearly 95 percent of the injected procaine can be found in the urine either as PABA, para-aminohippuric acid, para-aminobenzylglycuronate and DEA, or even as traces of procaine. Procaine or one of its hydrolytic products, PABA, has been shown to be removed from the blood stream in 20 minutes. It is thought that, in inflamed areas, procaine administered by the intravenous route has a two-fold action: (1) Direct action in the irritated nerve fibers; (2) indirect action of DEA on the endothelium of blood vessels. The basic structural similarity between DEA, benadryl, and choline must be noted. The mode of action, as with benadryl at the capillary bed, may be considered as a competition between histamine and DEA for a given site of action or receptive substance; or the action might be explained from the clinical observations on a cholinergic type response—*DEA* has an *anticholinesterase* action.

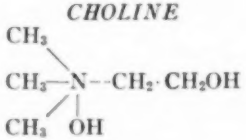
DIETHYLAMINOETHANOL



BENADRYL



CHOLINE



Structural relationship of DEA-benadryl and choline

Physiologic action

In order to simplify the giving of the procaine, "procaine unit" was devised which is the amount of procaine calculated at 4 mg. per kg. body weight to be given in 20 minutes in a 0.1-percent isotonic saline solution. One gm. of vitamin C is added to 1,000 cc. of isotonic saline solution containing 1 gm. of procaine hydrochloride.

During the administration—after about 5 minutes the patient usually describes a sensation of warmth over the entire body—a dryness of the mouth may be experienced.

In order to see what changes occurred in the normal eyes during and after its administration, 12 cases were studied as tabulated in Table 1. Although tearing of the eyes and dilation of the pupils has been reported with larger and more concentrated doses, neither reaction was observed in this series.

The pupils remained the same size and

TABLE 1

CHANGES OCCURRING IN NORMAL EYES DURING AND AFTER PROCAINE ADMINISTRATION

No.	Date	Name and No. of Injections	Chart No.	Age (years)	Condition for Which Procaine Administered	Weight and Dosage	Tension Before and 30 Minutes After Administration (mm. Hg Schiøtz)
1	1/11/48	M.O.	38478	58	Herniated disc	90 Kg.–360 mg.	O.D. 18; O.S. 18 O.D. 18; O.S. 18
2	1/11/48	J.D. (20)	38469	48	Dest. Arthritis of hips	70 Kg.–280 mg.	O.D. 18; O.S. 18 O.D. 18; O.S. 18
3	1/25/48	E.H. (7)	38502	61	Arthritis of knee	80 Kg.–320 mg.	O.D. 23; O.S. 23 O.D. 23; O.S. 23
4	1/25/48	R.K. (24)	38464	30	Arthralgia	58 Kg.–232 mg.	O.D. 22; O.S. 20 O.D. 20; O.S. 20 Aniridia, O.U. Nystagmus O.U. Post. polar cataracts O.U.
5	1/18/48	S.S. (10)	37042	56	Incipient gangrene	75 Kg.–300 mg.	O.D. 20; O.S. 20 O.D. 18; O.S. 20
6	1/18/48	I.B. (21)	37051	52	Scalenus anticus syndrome	48 Kg.–192 mg.	O.D. 20; O.S. 20 O.D. 18; O.S. 18
7	1/18/48	R.F. (9)	39023	52	Arthritis of hips	75 Kg.–300 mg.	O.D. 12; O.S. 12 O.D. 12; O.S. 12
8	1/18/48	S.Y.	37907	53	Rheumatic arthritis	70 Kg.–280 mg.	O.D. 15; O.S. 18 O.D. 12; O.S. 16
9	1/25/48	J.L. (2)	38492	30	Arthritis	100 Kg.–400 mg.	O.D. 18; O.S. 16 O.D. 17; O.S. 17
10	1/25/48	J.B. (3)	38512	58	Fractured fibula	90 Kg.–360 mg.	O.D. 12; O.S. 12 O.D. 12; O.S. 12
11	1/25/48	M.D. (7)	39022	43	Traumatic arthritis	85 Kg.–340 mg.	O.D. 17; O.S. 16 O.D. 15; O.S. 16
12	1/25/48	J.S.	38435	48	Concussion with paralysis of right lateral rectus	70 Kg.–280 mg.	O.D. 10; O.S. 12 O.D. 10; O.S. 12

continued to react normally consensually and to light and accommodation. There was no change in the size of the retinal vessels or other evidences of caliber variation. The tension showed no appreciable fluctuation, either during the administration or 30 minutes after.

From its physiologic action and chemical nature, on theoretical grounds, it seemed that in conditions in which vasodilation would be of value, procaine intravenously might be of ocular aid (figs. 1, 2, and 3). Accordingly, several cases of occluded retinal vessels were studied including one case of Buerger's disease with an occlusion of a superotemporal artery. No change was noted after treatment that could in any way be interpreted as related to the treatment. In like fashion, no improvement that could be attributed to the medication was noted in the treatment of five cases of branch thrombosis. Several cases of diabetic retinopathy were likewise treated with no effect whatsoever.

USE IN GLAUCOMA

In view of the anticholinesterase action of procaine, a reduction of intraocular pressure in some forms of glaucoma might theoretically be expected. Accordingly, 10

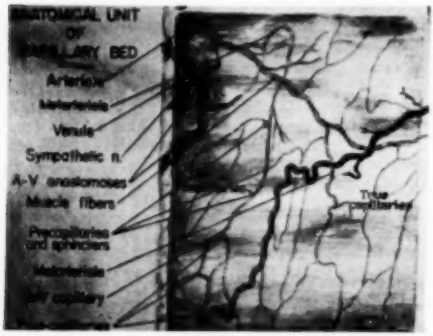


Fig. 1 (Givner and Graubard). Anatomy of capillary bed.

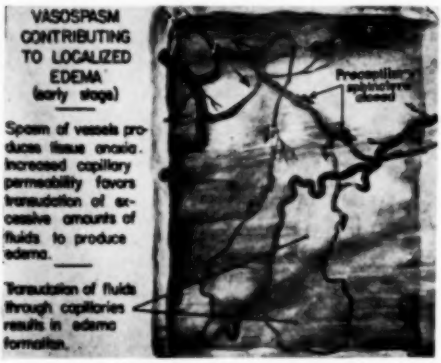

VASOSPASM
CONTRIBUTING
TO LOCALIZED
EDEMA
(early stage)
Spasm of vessels produces tissue anoxia. Increased capillary permeability favors transudation of excessive amounts of fluids to produce edema.
Transudation of fluids through capillaries results in edema formation.

Fig. 2 (Givner and Graubard). Formation of edema.

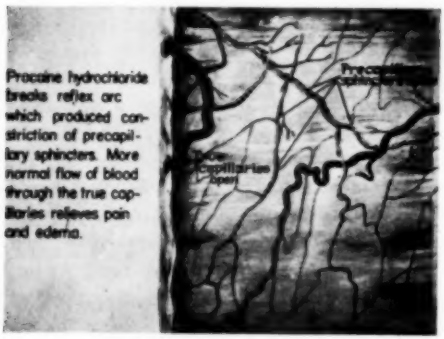

Procaine hydrochloride breaks reflex arc which produced constriction of precapillary sphincters. More normal flow of blood through the true capillaries relieves pain and edema.

Fig. 3 (Givner and Graubard). Mode of action of procaine.

cases of glaucoma (table 2) were investigated. Realizing that the drop in tension might not be noticeable until more than 30 minutes had elapsed, tensions were taken at 30-minute intervals for 2 hours after the administration of the procaine.

One might thus conclude that to date there seems to be no indication for the use of procaine intravenously in the treatment of glaucoma. Two cases of painful absolute glaucoma are, however, worthy of note. In these cases, there was marked relief of pain after intravenous procaine.

Case 1. H. S., a woman, aged 75 years, was a diabetic who had absolute glaucoma of the left eye. Vision was light perception and the unbearable pain could be controlled only little by the use of opiates. A cycloelectrolysis was done, as well as a retrobulbar alcohol injection, but the pain continued. After several weeks, enucleation was decided on but intravenous procaine was attempted as the last palliative. Pain was promptly controlled and, after three injections, no further injections were needed even though the tension remained high and no visible difference was seen by the examiner.

Case 2. N. Mc., a woman, aged 63 years, had a thrombosis of the central retinal vein of the right eye (incomplete) with secondary glaucoma. An iridencleisis had been performed, and the pain and tension were temporarily reduced. After sulfonamides were administered systemically for an infection not related to the operation, the tension rose again, hemorrhage appeared in the anterior chamber, and pain recurred and could not be controlled. The patient was given an intravenous procaine injection and experienced complete relief of pain. One other injection was given three days later, as a prophylactic measure against the recurrence of pain. The pain has not recurred (8 months). The patient had been using miotics previous to the onset of the pain and has used them subsequently. Following procaine administration, the tension was lowered to normal with miotics and has remained this way.

In one other condition, herpes zoster ophthalmicus, there was relief of pain after

TABLE 2

GLAUCOMA CASES TREATED WITH INTRAVENOUS PROCAINE

Date	Name	Sex	Condition	Initial Tension	Tension after Procaine		
					30 min.	1 hr.	2 hr.
2/4/48	M.A.	M.	Iritis with secondary glaucoma, O.D.	O.D. 18 O.S. 60	18 60	18 60	18 60
2/4/48	H.B.	M.	Aphakia with glaucoma, O.D.	O.D. 65 O.S. 18	65 18	65 18	65 18
2/19/48	M. Del.	F.	Chronic simple glaucoma (Irido-Corneosclerectomy had been done, O.U.	O.D. 30 O.S. 40	30 40	30 40	30 40
2/19/48	T.D.	M.	Chronic simple glaucoma, O.D.	O.D. 65 O.S. 23	60 20	65 23	65 23
3/4/48	H.L.	M.	Chronic simple glaucoma, O.D.	O.D. 40 O.S. 20	40 20	40 20	40 20
3/4/48	P.P.	M.	Chronic simple glaucoma, O.U.	O.D. 35 O.S. 40	37 42	35 48	35 45
3/18/48	F.D.	F.	Chronic simple glaucoma, O.U. O.D. absolute glaucoma	O.D. 55 O.S. 30	55 30	55 30	55 30
4/5/48	A.M.	F.	Incomplete thrombosis of central ret. vein., congested glaucoma, O.D.	O.D. 45 O.S. 20	45 20	40 20	40 20
4/6/48	F.S.	F.	Diabetic Absolute glaucoma, O.S.	O.D. 20 O.S. 50	20 50	20 50	20 50
4/6/48	M.M.	F.	Aphakic, O.D. Chronic simple glaucoma, O.D.	O.D. 30 O.S. 20	30 20	30 20	30 20

the administration of procaine intravenously (2 cases). The injection had to be repeated, since the beneficial effect was only temporary (lasting two days after one injection). However, this type of therapy can be safely added to our armamentarium in the handling of the pain in this condition.

SUMMARY

1. Administration of procaine intravenously has no effect on the intraocular pressure either in normal individuals or in patients with chronic glaucoma.

2. No beneficial effect followed the use of procaine intravenously in occlusion of retinal arteries, in diabetic retinopathy, or in five cases of thrombosis of retinal vein branches.

3. Some relief of pain followed the administration of procaine intravenously in the treatment of herpes zoster ophthalmicus. The relief was not permanent.

4. Marked continued relief of pain was experienced in one case of absolute glaucoma and one case of hemorrhagic glaucoma.

5. Further studies will be made to see if there are other indications for its use in ophthalmology.

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NOTES, CASES, INSTRUMENTS

LOCAL USE OF ANTISTINE IN NODULAR EPISCLERITIS*

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According to Duke-Elder,[1] "Nodular episcleritis is a disease of obscure origin, of recurring but benign habit, characterized by the appearance of a localized nodular inflammatory focus in the episcleral tissues. The nodule seems to appear suddenly, and is always surrounded by an area of hyperemia and vascular dilatation. The entire globe may show some generalized hyperemia, but it is never as marked as the region about the nodule."

ETIOLOGY

The etiology has never been satisfactorily explained, but the texts and the literature of the present and past persist in incriminating the famous triad—rheumatism, gout, and focal infection. On this basis the treatment has been directed to the alleviation of pain in which the use of salicylates has been the most popular.

The condition called episcleritis periodica fugax has undoubtedly been frequently confused with the nodular type. Here, too, Fuchs,[2] father of its name, listed rheumatism, gout, and so forth as the etiologic agents. Although a great similarity may exist, the clinical differentiation between the two conditions is characterized by the transient character of the latter and its marked tendency to recur with great regularity.

It is noteworthy that, in this periodic type, the role of allergy has long been suspected. The most prominent view implicates hypersensitivity to the tuberculoprotein. Cases have been reported that appear strongly suggestive of allergy, although their authors did not always bring this out too clearly.

Balyeat[3] reported a single case in 1932 occurring in a physician, who was "apparently" cured by avoidance of certain foods. These authors quote the work of Edward Jackson, who after a period of several years of study felt strongly concerning the possibility of allergy as the etiologic factor.

Shoemaker[4] reported two cases of episcleritis caused by the excessive use of carbohydrates. However, instead of suspecting allergy, the author concluded that the condition was caused by poisons formed in the gastrointestinal tract, due to faulty digestion and carbohydrate metabolism.

Sinskey[5] and his co-workers also reported a case of episcleritis due to faulty carbohydrate metabolism, and they concluded that dietetic factors should be considered in each case.

In the recent literature Shepherd[6] reports five cases of episcleritis wherein the pain was relieved by the local instillation of histamine diphosphate. No attempt at etiologic correlation was made.

USE OF ANTISTINE

Because of the gratifying results obtained with the use of Antistine (Ciba) locally in a large series of known allergic eye disorders, it was deemed worthwhile to examine the effects of this drug.* The chemical known as Antistine hydrochloride† is the trade name for phenazoline hydrochloride, which is a synthetic preparation. It is made up in ophthalmic solution to a 0.5-percent concentration bearing a pH of 6.94.

Antistine was apparently first used internally at the University of Basel, and was found to be a useful antihistaminic in the

* From the Department of Ophthalmology, Marquette University Medical School.

* Grossmann, E. E., and Hitz, J. B.: To be published.

† The material used in this study was furnished by the Ciba Pharmaceutical Company, Summit, New Jersey.

treatment of allergic diseases by Schindler[7] and Brack.[8] The ophthalmic solution was apparently first used by Bourquin,[9] who reported its use in 37 cases, many of which were nonallergic. As far as is known there is no specific report concerning its use in the treatment of nodular episcleritis.

In episcleritis

A total of 22 patients whose conditions were diagnosed as episcleritis were treated by topical instillations of Antistine. In each case the clinical picture was characterized by a sudden onset of deep injection of a quadrant or more of the globe and with well-marked pain. There was a definite, elevated yellowish or grayish yellow nodule surrounded by intense redness and hyperemic blood vessels.

In the series of cases treated, only 3 patients admitted to having had a previous attack, 2 cases of which were in the opposite eye and were treated by this method; the other 19 patients were positive in their assertions that the present episode was the initial one. Two of these 3 are known tubercular patients.

Patients were instructed to instill the solution into the affected eye by eye dropper every three hours, and were told to return daily for further observation.

Results

Of the total treated, 17 were men and 5 were women. The ages varied from 20 to 57 years. The apparent disproportion in sex distribution is accounted for by the unusually high proportions of men patients seen at this institution.

TABLE 1

Subjective relief obtained with Antistine therapy in nodular episcleritis

Symptomatic Relief (Time)	Number of Patients
24 hours	3
24–72 hours	11
3 to 7 days	7
No relief	1

Noticeable relief in symptoms were obtained in all patients except one, as shown in Table 1. The patients were thoroughly questioned concerning this subjective relief, and there seemed no doubt that the element of pain had disappeared. Clinically the cure was noticeably less dramatic; yet the redness and the nodular elevation subsided within a few days after symptomatic relief (table 2).

Of the 22 cases, 7 were diagnosed as pulmonary tuberculosis (the one failure occurred in this group), 1 had an associated rosacea keratitis, 1 had an undiagnosed skin disease, and 13 had no associated disease.

TABLE 2

Objective improvement obtained with Antistine therapy in nodular episcleritis

Objective Improvement	Number of Patients
1 to 3 days	8
3 to 5 days	4
5 to 7 days	7
7 or more days	2
No improvement	1

Conclusions

The use of the antihistaminic known as Antistine has shown to be highly efficacious in the treatment of nodular episcleritis. Of a total of 22 cases, 14 obtained dramatic relief from pain within 3 days, and 21 of the 22 were relieved in 7 days. Objective improvement was noted to be somewhat slower, the greatest improvement occurring in from 5 to 7 days after treatment.

The use of the antihistaminic was suggested by the inferences in the past literature concerning the possibly allergic etiologic factor in nodular episcleritis.

The local use of the drug was deemed to be the best method of application in view of the work by Friedlaender and Feinberg[10] suggesting that failure of relief when antihistaminics were used was due to insufficient drug reaching the site of action.

238 *West Wisconsin Avenue.*

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CIRCINATE DEGENERATION OF THE RETINA*

With report of a case

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Circinate degeneration of the retina is the term preferred by Duke-Elder for the disease originally described by Hutchinson, in 1876, as retinitis circinata. It was thoroughly reviewed by Edgerton in 1936 and another case reported by him.[1]

Since Edgerton's review, reports on seven more cases can be found in the literature. J. Margenot,[2] in 1936, reviewed the pathogenesis in two cases. M. Handmann,[3] in 1937, reported a case in a woman, aged 49 years, which he had observed for five years, from its incipient stage until the development of the white, degenerated area.

Two cases reported by Jules François[4] showed a retinal degeneration which began following thrombosis of the macular veins. The thrombosis preceded by several months the development of the retinal degeneration.

Holden[5] presented the case of a woman, aged 58 years, who had diabetes and high blood pressure. There were both old and new hemorrhages in the involved areas of the retina. S. Holm,[6] in 1941, reported the case of a woman, aged 82 years, in whom the eye was enucleated, but the suspected neoplasm was not found. In this case, the principal microscopic changes found were: increase in pigmented cells, some in massed formation and others scattered throughout the degenerating tissue; changes in the arrangement of rods and cones in some places, and, in others, the entire loss of rods and cones; round-cell infiltration of the retinal vessels.

Rebelo,[7] in 1943, reported a case in which there were discreet hemorrhagic areas within the ring of degenerating retinal tissue. His observation of normal appearing retinal vessels coursing uninterruptedly over the white areas of degeneration is in accord with the observation of most authors on this point.

One case in a child has been reported since Edgerton's review in 1936. This was reported by Morgan in 1944.[8] This case was in a boy, aged 8 years, in whom the chief complaint was reading difficulty. He had vision of 6/18 in the right eye and 6/5 in the left. There was a history of concussion at seven years of age with bruises over right side of head, so that the right eye was closed. No definite etiology could be established in this case and the concussion could only be referred to as a possible cause.

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CASE REPORT

History. The case to be reported here occurred in a man, aged 57 years. He came to me first in May, 1947, on account of an acute blepharitis and conjunctivitis. He also complained of poor vision in his right eye. He had had his eyes tested for glasses one year previously but no mention was made by the examiner of any visual defect.

Vision was: R.E., counts fingers at 15 inches; L.E., 6/6−3. He gave a history of some prostatic involvement, but his general physical examination was otherwise essentially normal. Blood pressure was 165/85 mm. Hg, with urine negative for albumin and sugar, and Kahn test negative.

External eye examination. Mild, acute blepharitis of both eyes and a small chalazion in the left upper lid were present. There was acute conjunctivitis of both eyes. The pupils were regular, 3 mm. in diameter, and reacted normally to light and accommodation. The corneas were clear. Tension was normal in both eyes.

The ophthalmoscopic examination of the right eye was as follows: The cornea, lens, and vitreous were clear. The optic disc was sharply outlined and of normal appearance. There was marked tortuosity of some of the smaller veins and along the superior temporal vein were tortuous, dilated small veins, resembling clusters of grapes and occasionally punctate hemorrhages from these clusters. The retinal tissue immediately surrounding the macula was cloudy, with several punctate hemorrhages in the macular area. The macula was girdled by two semicircular arcs with open spaces at the nasal and upper temporal ends. The lower arc was wider in its middle portion, approximately 1½ times the diameter of the optic disc, and tapering somewhat toward both ends. This lower arc was yellowish white in color throughout its entire extent and had numerous small, rounded, discreet spots of a silvery sheen scattered over its surface. Its borders were irregular in outline, as though numerous smaller white spots had coalesced.

In the upper arc, the temporal half was yellowish white in color, but more narrow than the lower arc. The nasal half was a mottled slate gray in color and composed of numerous rounded, discreet patches which had not yet coalesced and were evidently of more recent origin. Coursing over this entire degenerated area, retinal vessels could be seen clearly outlined. There were numerous punctate hemorrhages, especially along the superior temporal vessels and in the region of the gray inner end of the upper arc.

In the left eye, the media were all clear, except for a few small vitreous opacities. The retinal vessels also showed some sclerotic changes. The fields of vision in both eyes showed a normal peripheral field. In the right eye, there was a large central scotoma.

This retinal degeneration occurred in a man in whom no general physical condition could be found as a possible etiologic factor.

The inner, upper portion of the degenerating retina was evidently the most recent part to be affected and it was in this region where most of the punctate hemorrhages were noted and in which the tortuosity of the veins was most marked.

Comment. Many other reports have noted the occurrence of hemorrhage as the probable beginning of the circinate degeneration, and it is probable that some degree of arteriosclerosis occurs in the majority of the cases occurring in elderly people. The fact that an occasional case is seen in children and young adults would indicate that, at times, factors other than arteriosclerosis are responsible.

In the case here reported, hemorrhage and sclerotic changes in the retinal vessels are the predominant findings, and it seems reasonable to assume that they were the prime factors in producing the degeneration noted.

Course. This patient was seen again in

May, 1948, approximately one year following the original examination. The only change to be noted in the period of one year was an increase in the density of the white portion of the upper arc of the degenerating area. This change is further evidence that the upper arc is the portion of the retina most recently involved. Also that

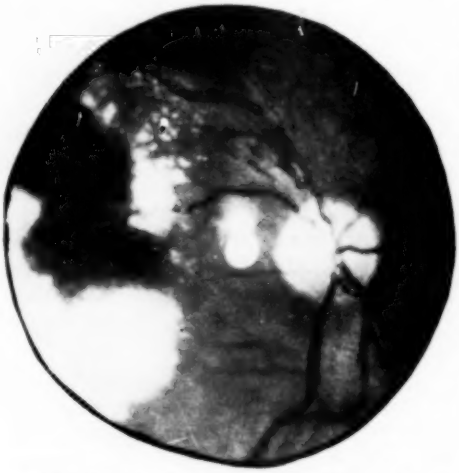

Fig. 1 (Henderson). The white, degenerated area is not elevated above the surrounding retina but retinal vessels course evenly across its surface.

hemorrhage was of prime importance in the etiology, since it was in the proximity of this area in which most of the punctate hemorrhagic spots were noted.

Discussion

In making a diagnosis in this case, it is necessary to rule out the possibility of angiomatosis retinae, which may be found in a great variety of retinal manifestations and which is sometimes accompanied by a circinate degeneration.

The appearance of the upper temporal vessels (fig. 1), which were described as resembling clusters of grapes, leads one to a careful inspection of the fundus periphery for other evidence of angiomatosis.

There are no sacculations or aneurysmal dilatations, such as described by Duke-Elder and others.

The white, degenerated area is not elevated above the surrounding retina but, as can be seen from the photograph, retinal vessels course evenly across its surface. The retinal vessels, other than those seen in the upper temporal area, while considerably dilated, show no evidence of aneurysmal dilation and none of them end in a sacculation.

The preponderance of reports of angiomatosis are in young adults, the preference being in the third decade.

In the present case, there is definitely a lack of the extensive and marked vascular changes, or evidence of tumor formation or massive retinal exudate, which are more characteristic of angiomatosis.

1200 Central Avenue.

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SILVER NITRATE CAUSING DACRYOCYSTITIS

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For the prophylaxis of ophthalmia neonatorum, silver nitrate instillation is a routine procedure. In ophthalmic textbooks, old and new, no mention is made of silver nitrate solution as an etiologic factor in the production of dacryocystitis in cases of nasolacrimal duct obstruction. That such a factor exists is suggested by several observed cases.

REPORT OF CASES

CASE 1

Bilateral nasolacrimal duct obstruction. T. R. was seen at the age of 5½ weeks. Silver nitrate, 1 percent, was instilled following birth. On the fifth day, acute purulent discharge in the right eye occurred, followed by a similar involvement of the left eye. In both eyes there was lid edema, marked conjunctival injection, profuse purulent discharge, purulent expression from the puncti, and an extensive superficial central keratitis. Bilaterally, the ducts were obstructed. Dilatation of the puncti, irrigation with penicillin, and probing of both ducts established drainage. The course thereafter was uneventful.

CASE 2

Unilateral nasolacrimal duct obstruction. P. M. was seen at the age of 7 days. Silver nitrate, 1 percent, was instilled after birth. On the fifth day following birth, the left eye became involved. Lid edema, marked purulent discharge, purulent expression from the punctum, and several small corneal punctate staining areas were observed. The nasolacrimal duct was not patent. The course after probing of the duct was unremarkable.

Ten additional unilateral cases were observed within seven days after birth. Except for the absence of corneal involvement, all were similar in severity with uneventful courses following reëstablishment of duct patency.

CASE 3

Unilateral duct obstruction. P. A. was seen at the age of 7 months. Epiphora of the right eye was present shortly after birth. Signs of duct inflammation were at no time present. Irrigation of the duct system revealed complete obstruction.

Following the irrigation, experimentally, one drop of 1-percent silver nitrate solution was instilled. On the third day, a moderate amount of silver catarrh was present, the cornea being clear. Upon irrigation of the sac, considerable white, stringy, clumpy debris was obtained through the puncti.

After probing of the duct, the course became uneventful.

COMMENT

The coincident occurrence of dacryocystitis in nasolacrimal duct obstructions alerts one to the likely implication of the nitrate of silver solution. Normally, silver nitrate solution is said to be neutralized rapidly by the chlorides in tears. A deficiency factor, influencing considerably the pathologic process—a deficiency in the defense against bacterial invasion—is the absence of tears at birth. Inadvertent instillation of strong silver solution into the eyes of newborn infants, or failure in the neutralization of the instilled drops, may form the basis of the complication.

Prophylactically, to minimize the danger to the nasolacrimal duct system, neutralization by and generous irrigation with normal saline solution should follow nitrate of silver instillation. This neutralization and irrigation would be especially desirable after use of those solutions which, unknown to the user, have increased in concentration.

It seems possible that the dacryocystitis observed in newborn infants with nasolacrimal duct obstruction may be the result of nondrainage through of the silver nitrate solution and its subsequent caustic action on the mucous membrane of the lacrimal system.

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A SIMPLIFIED ASTIGMOMETER*

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Chicago, Illinois

Precision in refraction requires that the axis and value of any cylinder needed be known before dealing with the spherical correction. The reverse routine, by which the sphere that gives the best vision is first determined and the weakest acceptable cylinder then added, does not assure an exact correction even under cycloplegia. The final result of such technique is not infrequently an undesigned spherical equivalent. To attain the sharpest possible focus, the correct cylinder, regardless of power or axis, must be prescribed. Toleration will ensue if compensation is provided for associated factors, such as the differential prismatic action of the lenses or persisting accommodative tone, though, or course, the patient may require some days to reinterpret the new type of imagery and "get used to the glasses."

All methods of cylinder determination have their place but one of the most generally useful is the astigmatic chart. It is invaluable in noncycloplegic and postcycloplegic refraction, and likewise is a desirable check after cycloplegic retinoscopy. Moreover, when adequate objective refraction is impossible, as in opacities of the cornea, conical cornea, and incipient cataract, the astigmatic chart often gives helpful results.†

The ideal astigmatic chart should be a single unit of simple design, easily handled, unsoilable, and need no computation. The projectochart cross dial, although excellent otherwise, fails in the last qualification. The correct use thereof is also rather complicated. After proper fogging, the cross is set at axes 90° and 180°. If the lines look alike either no astigmatism is present or the axis is 45° or 135°. If the vertical line is clearest, as will be assumed, the axis may be 90° or within 45° to either side. The cross is then rotated 45°. If the line at 45° is clearest, the 45° meridian must be closer to the true axis than that at 135°. As the clearer line is rotated step by step away from 90°, the difference between the two lines lessens until at a certain point both lines have the same appearance. If this position is 30°, the true axis is 45° therefrom or at 75°.

ASTIGMOMETER OF NEW DESIGN

All this computation is avoided in the dial of my design which I appropriately term "a simplified astigmometer" (fig. 1). Incidentally, the word astigmometer, though perchance unfamiliar, is in the unabridged dictionaries, the definition being "an ap-

* From the Department of Ophthalmology, Northwestern University Medical School. Read before the Chicago Ophthalmological Society, March 21, 1949. The instrument described is made by Belgard, Inc., 109 North Wabash Avenue, Chicago 2, Illinois.

† Illustrative cases: (a) Woman, aged 31 years. Paracentral scars left cornea. Glasses from oculist, one month old: L.E., +1.25D. sph. ⌒ −3.0D. cyl. ax. 95° = 20/30. Prescription after astigmometer test (postcycloplegic)): L.E., +0.25D. sph. ⌒ −4.0D. cyl. ax. 95° = 20/20. (b) Girl, aged 12 years. Bilateral conical cornea. Oculist reported after cycloplegic refraction uncorrectible amblyopia: R.E., −0.5D. sph. ⌒ +5.0D. cyl. ax. 10° = 20/70; L.E., −0.50D. sph. ⌒ +4.50D. cyl. ax. 170° = 20/100−1. After the astigmometer test the indicated prescription was: R.E., −1.0D. sph. ⌒ +8.0D. cyl. ax. 5° = 20/30; L.E., −5.75D. sph. ⌒ +7.0D. cyl. ax. 175° with 4.5△ slab-off, 20/40. Although this would have given serviceable vision, contact glasses were advised, and an excellent result was reported. (c) Man, aged 70 years. Immature cataract, left eye. Glasses from oculist, six weeks old: L.E., +0.75D. sph. ⌒ +0.75D. cyl. ax. 180° = 20/200. After astigmometer test prescribed: L.E., +2.0D. sph. ⌒ +2.0D. cyl. ax. 10° = 20/30.

paratus for measuring the degree of astigmatism."

This new chart is durably made of vinylite plastic and hence maintains permanently its cleanliness and contrast. The axes are indicated with dual numbering completely around the dial. The outer figures are read when the dial is seen in the mirror while, with direct vision, the inner figures in parentheses are noted. The use of the dial with a mirror facilitates considerably the examination, and is highly recommended. If the convenient roller acuity chart is used, a nail at the top of the box can serve when needed to hold the astigmatic dial. In a lightly decorated examining room the general illumination is usually adequate enough for the astigmatic test. Additional local illumination when required on account of poor discrimination can be provided by the Sphero-Lux or similar examining lamp. Clinical experience has shown that the single-line cross is most suitable for the determination of cylindrical power. For the location of the axis the rotating Maddox V is more efficient since the astigmatic eye can distinguish best a difference between two lines at an angle of 60° (Verhoeff). By placing an inverted V as an arrowhead over one line the two designs are neatly combined and the astigmometric procedure is greatly simplified. The arrowhead is used to indicate the cylindrical axis; the cross to determine the cylindrical power. The chart design thus consists simply of two long lines making the cross and two short lines forming the arrowhead, all of an even 5-mm. width.

Use of dial

In using this dial, the eye is properly fogged and the cross lines are presented at axes 90° and 180°. If the lines look alike and the wings also match, no astigmatism is present. But if the wings do not match the axis is 45° away on the side of the lighter wing. On shifting the arrow to this position, the arrow-line will be the blacker of the two principal lines. If, in the primary position of the cross, the clearest line is vertical, the arrow is pointed to 90°; if horizontal, to 180°.

The attention is now directed to the arrowhead. If the wings match, the axis, as indicated by the shaft, is correct. If one wing is blacker, the arrow is rotated *away* from the blacker wing until matching ensues.

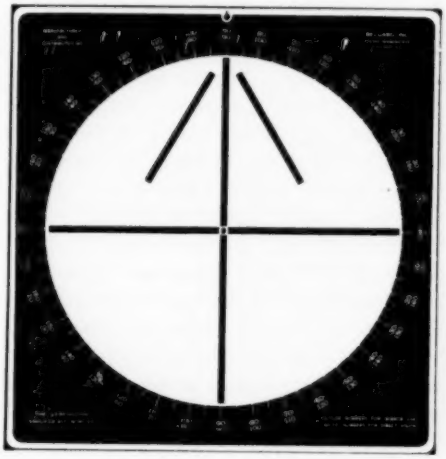

Fig. 1 (Lebensohn). A simplified astigmometer.

Where this occurs, the arrowshaft is at the correct axis and no further computation is necessary. To illustrate: if the clearest line is horizontal and the lower wing blacker, the arrow is moved upward until the wings look alike. Should the arrow be rotated beyond the neutral point, the upper wing will be clearer, an indication that the movement must be reversed somewhat.*

After the axes are located, the cylindrical power is next determined. The arrowhead now serves as a distinguishing mark by which the arrow-line or the other can be identified. Minus cylinders are placed at right angles to the arrow-line until this line,

* When the astigmatism is of such high degree that the wings of the arrow cannot be distinguished, the position of greatest clarity of the one line seen can still be determined. The patient usually notes a change in blackness and sharpness as this line is rotated in steps of five degrees in one or other direction.

at first the clearest, is matched by the other. If the fogging is adequate the next 0.25D. stronger cylinder should reverse the contrast.

With the cylindrical correction worn, the fog is gradually reduced in turn from each eye until no further visual improvement occurs. The position of the axis is then checked by the effect of the cross-cylinder on the Snellen letters, using the 0.12D. instrument for a corrected acuity of 20/20 or better, the 0.25D. model for a correction of 20/25 or less. If this test indicates a divergence from the axis found with the astigmatic dial, the exact axis direction can be decided by the Crisp-Stine test for which the arrow-line is ideally adapted.

Crisp-Stine test

The use of the Crisp-Stine test can be explained best by an illustrative case. Assume that the provisional correction is: R.E., +1.0D. cyl. ax. 15°, 20/20. With the letter chart, the cross-cylinder indicates apparently an axis of 30°. The eye is fogged 0.25D. and both the trial cylinder and the arrow-line are placed at 15°. The 0.12D. cross-cylinder is applied in the test for axis and the query is whether the wings look more alike before or after the turn of the cross-cylinder.

If the wings seem alike with the plus mark of the cross-cylinder up, *both* the arrow-line and the trial cylinder are moved to 25°, and the test reapplied. If now the wings appear matched with the plus mark of the cross-cylinder down, the correct axis is 20°. When both the arrow-line and the trial cylinder are moved to this position, application of the cross-cylinder test will show a contrast in the wings that is reversed on rotation of the instrument.

The average fog should be about 0.75D. For cycloplegic cases the proper fog is attained by algebraic addition of the sphere and cylinder found in retinoscopy at one meter. When the arrow-line is placed in the axis of the plus cylinder, the appearance of the arrowhead will signal what change in axis position is required. In presbyopic cases, the glasses worn should be measured and the corrected acuity noted. Then a slip-on occluder is placed over one lens. The desirable fog is determined by placing over the other a plus sphere from the trial case of 1.0D. or more as indicated. In postcycloplegic testing +0.5D. sph. is added to the previous cycloplegic findings before the check for cylindrical power. Subsequently, after the fog is adequately reduced, +0.25D. sph. is added and the accuracy of the axis is checked by the Crisp-Stine test.

It is sincerely hoped that the simplified use of the astigmatic chart which I have described will help to extend the popularity that this technique deserves.

4010 West Madison Street (24).

I am indebted to my gifted resident, Dr. Warren W. Kreft, who made by hand with great pains the experimental plastic model of the instrument.

SOCIETY PROCEEDINGS

Edited by DONALD J. LYLE, M.D.

NEW YORK SOCIETY FOR CLINICAL OPHTHALMOLOGY

November 1, 1948

DR. BENJAMIN ESTERMAN, *president*

CORRELATIONS BETWEEN OPHTHALMOSCOPY AND HISTOPATHOLOGY

DR. BERTHA A. KLIEN, Northwestern University Medical School, Chicago, discussed this subject during the instruction period.

RECURRENT UNILATERAL GLAUCOMA WITH CYCLITIC SYMPTOMS (case of the month)

DR. ISADORE GIVNER presented the case of a man, aged 43 years, whose right eye had been painful and red for 10 days. Past history showed recurrent attacks of similar nature. A diagnosis of glaucoma had been made and the patient had used pilocarpine during the previous attacks. The patient stated that for many years he had had a fever in the afternoon, fatigue not related to exercise, and attacks of diarrhea. He had spent time on a farm many years ago where unpasteurized milk was drunk. X-ray studies of the chest and the Wassermann test were negative.

Examination of his eyes revealed that the right pupil was larger than the left, and there were many keratic precipitates on the posterior surface of the cornea of the right eye. The intraocular pressure was 37 mm. Hg (Schiøtz) in the right eye and 20 mm. Hg in the left. The peripheral fields were normal and the blindspot of the right eye was enlarged. Six days later, after using pilocarpine (2 percent) 3 times a day, the tension was 25 mm. Hg in the right eye. Following skin testing for brucellosis, 8 days previously, all keratic precipitates disappeared. The tension of the right eye was 18 mm. Hg with and without pilocarpine. The patient discontinued drops and the tension remained at 18 mm. Hg, and vision was 20/15, with no symptoms.

Dr. Givner said that he wished to submit the following questions for discussion:

1. He asked Dr. Conrad Berens, what is the relationship, if any, of systemic disease to primary glaucoma?

2. He asked Dr. Harold Harris whether the evidence cited was sufficient to establish a diagnosis of brucellosis?

3. He asked Dr. Adolph Posner if he felt that this was a case of glaucomatocyclitic crisis described by Posner and Schlossman; if so, what is its position in the classification of glaucoma?

Discussion. DR. CONRAD BERENS replied to the question that undulant fever has been regarded as a cause of chronic uveitis by many investigators, notably by Orloff, who reported two cases of undulant fever with extensive ocular complications, and produced experimental keratitis, uveitis, and neuroretinitis in guinea pigs by inoculations with Brucella abortus. Green also observed 4 cases of undulant fever, and collected from the literature 28 additional cases with such ocular conditions as keratitis, uveitis, retinitis, and optic atrophy.

In studies at Cornell University, agglutination and skin tests for undulant fever were carried out on 57 patients. Because it is often difficult to make a clinical diagnosis in the subacute or chronic forms of undulant fever by the isolation of brucella organisms, immunologic procedures, such as agglutination, intradermal or complement fixation tests, and opsonocytophagic reactions are used. The interpretation of these tests were clarified in 1933 by Huddleson, Johnson, and Hammann and more recently by Harris. Since the intradermal and agglutination tests were considered to be the most reliable

tests for determining the existence of brucella infections, these tests were used at Cornell University.

Agglutination and intracutaneous tests were made on 25 patients with uveitis, 32 with other inflammatory eye diseases, and 6 with noninflammatory ocular lesions. Only one patient with chronic conjunctivitis had a positive agglutinin titer of 1:40; the intracutaneous reaction, however, was negative.

Of 57 patients, 3 had positive skin tests —2 with uveitis, and 1 with endophthalmitis. These patients were known to have used raw milk in their diet. The fact that the large majority of the tests were negative indicates that Malta fever did not play a significant role in this group of patients. However, most of the group were residents of a metropolitan area where only pasteurized dairy products were used.

Since these studies were made, Dr. Harris has examined many patients and, although some have apparently benefited from treatment with brucella antigen, only two have had severe ocular reactions. Dr. Berens said he believed that these two cases were quite certainly caused by brucellosis.

The last patient, who had bilateral uveitis, had a very severe ocular reaction. The vision was reduced to hand movements in the right eye and 10/200 in the left eye two days after a small dose of brucella antigen. This patient's condition did not respond to 25 gm. of dihydrostreptomycin. Dihydrostreptomycin is considered to be one fourth as toxic for the eighth nerve as the ordinary streptomycin and the patient has had no unpleasant symptoms or reactions.

After giving this treatment over a period of 10 days, combined with three intravenous injections of typhoid-H antigen, the anterior chambers of both eyes were aspirated and, two days following this treatment, there was considerable improvement in the left eye but the right eye gained little, if any, in vision or field. Following two blood transfusions, both the right and left eyes improved.

In spite of the fact that there was no specific proof that the treatment with brucella antigen was specific in any particular case, there were patients who had marked improvement after receiving brucella antigen. Therefore, for patients who show positive tests for brucellosis by experienced observers, the treatment with brucella antigen certainly is to be considered a worthwhile addition to our armamentarium in treating this disease.

What effect the intradermal testing had in apparently curing Dr. Givner's patient is difficult to say. However, Dr. Berens said that, in his experience, the cure of chronic uveitis by a single treatment with any antigen or by any other method has never occurred, although the first or second intradermal injections often cause a marked improvement. Dr. Berens asked Dr. Givner whether he thinks that this patient may have had so-called primary glaucoma for several years and that this attack was merely a subacute attack of uveitis from some cause other than brucellosis in a patient who had had recurrent attacks of glaucoma.

However, the fact that in 38 of 437 eyes the pathologic diagnosis was uveitis and the clinical diagnosis was chronic primary glaucoma makes one suspect that we often fail to recognize glaucoma as secondary to uveitis. The history and Dr. Harris's tests seem to be highly suggestive of the correctness of the diagnosis, but as in many cases it is difficult to say whether nature or our treatment was responsible for affecting a cure.

Another point in this case is unusual and that it is the almost immediate control of the tension with a 2-percent pilocarpine solution. Dr. Berens said that he usually has to try homatropine and cocaine and alternate these drugs with pilocarpine and the use of neosynephrin. In chronic or recurrent cases it is usually necessary to inject nonspecific protein and follow aspiration with atropine before tension is controlled. This seems to be another point in favor of the possibility

of a subacute attack of uveitis, not necessarily due to brucellosis.

DR. HAROLD HARRIS said that this man had an ocular condition which could be caused by a Brucella allergy. There was a history of ingestion of raw milk prior to 1915. About 1927 he began to have afternoon fever of unknown origin, accompanied by fatigue. In May, 1948, tests for brucellosis showed the following significant findings: Slight relative lymphocytosis with a total white count of 6,800, a so-called positive opsonocytophagic reaction, and a very weakly positive skin test. All other tests were negative. Eight days after skin testing all intraocular signs had disappeared. Seventeen days after the first opsonocytophagic test, a second test showed a moderate increase in phagocytosis of Brucella.

The evidence was insufficient to establish or rule out a diagnosis of brucellosis. However, it is not uncommon for pathologic processes of various types to clear up rapidly following the desensitizing effect of intradermal Brucella antigens, as may well have happened in this patient. Prolonged observation would be necessary, in view of the equivocal nature of the laboratory data, in order to clarify the diagnosis.

DR. ADOLPH POSNER said that this case is interesting because it opens to discussion the basic question: What is the nature of glaucoma, on one hand, and of cyclitis, on the other.

Glaucoma is generally classified into primary and secondary. Clinically such a classification is of little use and serves to stifle further thinking and research. To revert to the case presented, Dr. Posner posed three questions to be discussed:

1. Is brucellosis an etiologic factor?
2. Is the glaucoma primary or secondary?
3. How is the cyclitis related to the glaucoma?

Dr. Posner said that there was little he could add to the discussion given previously on this question except to mention that he had observed very similar clinical cases who gave negative results to brucellosis tests as well as to all others.

The second question loses much of its significance when it is realized that we have adopted arbitrary criteria in classifying glaucoma into primary and secondary. It is only by maintaining an open mind and by carefully observing and analyzing all the delicate nuances of each individual case that we can hope to learn more about the many different diseases which we include under the generic term of "glaucoma." By such a discriminating study, we may ultimately break down this heterogeneous group into several clinical entities.

One such entity, represented by only a small number of cases, appears to have been isolated by Barkan, Sugar, and Kronfeld as "narrow-angle glaucoma." The acceptance of "narrow-angle glaucoma" as an entity does not imply that glaucoma should be classified into narrow- and wide-angle glaucoma. Wide-angle glaucoma still remains a heterogeneous group of diseases of unknown etiology and the term is therefore meaningless.

In May, 1947, Dr. Posner said that he and Dr. Schlossman presented a group of 9 cases similar to the one described by Dr. Givner. This was believed to be another clinical entity and was called "the syndrome of recurrent glaucomatocyclitic crises." Dr. Posner said that he felt that the case presented belongs to this group.

The third question, that of the relation between the glaucoma and the cyclitis, has not been fully elucidated. That a relationship does exist is apparent from the fact that the keratitic precipitates disappear soon after the subsidence of the ocular hypertension. Both the glaucoma and the hypertension may be a result of an increased permeability of the capillaries in the ciliary body, or to a change in the ciliary epithelium itself. It may be related to an allergic response, although local and systemic administration of the antiallergic or antihistaminic drugs have thus far failed to produce a significant response.

Dr. Posner said that he agreed with Dr. Berens that pilocarpine does not always help, and other drugs may have to be tried. He said that he has never had to resort to paracentesis or other forms of surgery.

In these cases it is possible for keratitic precipitates to appear occasionally without a concomitant rise in ocular tension. In some of the cases, individual attacks of glaucoma have been noted in which cells and keratitic precipitates have remained absent. Such attacks assume all the earmarks of primary glaucoma and have been treated as such without bad effects.

This entity thus takes on an importance out of proportion to its actual incidence. It may well be that certain cases of primary glaucoma are related to this syndrome, so that it may be regarded as an intermediate link between primary and secondary glaucoma.

General discussion. Dr. Ludwig von Sallmann said that he felt that this case belonged to the group of cases known as recurrent glaucomatocyclitic crises. He suggested that the use of antihistaminics or pituitrinlike drugs might be beneficial. He said that Dr. Givner did not mention whether this case had attacks of cyclitis with cells in the anterior chamber without increased tension and at other times had a rise in tension without appearance of cells in the anterior chamber. He said that he agreed with Dr. Posner's views on the classification of primary and secondary glaucoma.

Dr. Frank Vesey asked why the investigation of this case was limited to brucellosis and whether any tests had been done for tuberculosis.

Dr. Arthur A. Knapp asked whether there was any systemic disturbance, whether an ear, nose, and throat examination was done, and whether the sphenoids had been irrigated.

Dr. Benjamin Esterman asked whether this case could be one of simple glaucoma with coincidental uveitis, and whether any provocative tests were done.

Dr. Adolph Posner replied that to determine whether it is primary glaucoma it is necessary to observe the case over future attacks. The provocative tests, water tests, and Lambert-Bloomfield tests give only positive results in simple glaucoma. Homatropine and dark-adaptation tests give positive results in narrow-angle glaucoma. This does not seem to be a case of narrow-angle glaucoma.

Dr. Isadore Givner said that he had presented only the positive findings in describing this case. X-ray studies of the sinuses and teeth were negative, and there was no infection of any kind found. X-ray studies of the chest to eliminate the possibility of tuberculosis were made and proved to be negative. The sphenoids were not washed since there was no indication for such a procedure, and the angle was perfectly normal.

Clinical and Histopathologic Aspects of Angioid Streaks

Dr. Bertha A. Klien, Northwestern University Medical School, Chicago, (by invitation) said that the main fascination of histopathologic studies lies in the ultimate possibility of finding explanations for all clinical manisfestations of disease. No other condition lends itself more readily to the correlation of a great variety of clinical and histologic phenomena than angioid-streak formation, mainly because of two circumstances. First, the clinical picture is characteristic and the clinical diagnosis definite from the earliest stage of just a few streaks around the optic disc to the advanced lesion with loss of central vision due to the disciform macular degeneration. Second, the course of the disease is very chronic, lacking the incidental tissue reactions of acute and subacute processes, every phenomenon being inherent in the pathogenesis of the disease.

The various phenomena occurring with angioid-streak formations are most easily discussed under two headings: (1) Find-

ings, which underlie clinically visible streak formation; (2) findings that underlie the peculiar appearance of the remaining fundus which is present in all advanced cases of angioid streaks and which consists of diffuse yellowish and diffuse opaque grayish discolorations.

Clinically, the earliest streaks are reddish brown with sharp, ragged outlines. Choroidal details are often visible within the broadest portions. Histologically, they are simple breaks in Bruch's membrane, rendered visible by the opacification of this membrane through elastic degeneration and calcification. Pigment epithelium and choroid are intact.

Old streaks often appear more yellowish or have yellowish-white accompanying lines. Histologically, many of the old defects of Bruch's membrane are filled with fibroblastic granulomas, which have formed around displaced, calcified fragments of Bruch's membrane. Other breaks are accompanied by linear crests of new tissue, which often undergoes hyalin degeneration. Injury of capillaries by sharp, calcified fragments of the membrane often leads to hemorrhages.

The pathologic process underlying the diffuse opaque yellowish or grayish areas consists in extensive new formation of a cuticular substance similar to the cuticular portion of Bruch's membrane but many times thicker. These cuticular deposits are often found over multiple breaks of the membrane, as if nature had attempted to preserve its continuity, so necessary to a normal pigment epithelium. The absence, presence, or hypertrophy of the pigment epithelium over these cuticular deposits produce their varied clinical appearance.

In the late stages of the disease the macular area is invariably occupied by a lesion, which has the typical clinical and histologic appearance of a disciform degeneration. The causes for the breaks in Bruch's membrane, however, are obvious, while they are still obscure in the Kuhnt-Junius type.

The pathogenesis of angioid streaks is based upon an abnormal fragility and opacification of Bruch's membrane. The fully developed picture, however, represents not only the visible ruptures of this membrane but also the multiform end results of irritation of pigment epithelium and choriocapillaris by the sharp, calcified edges and fragments of the broken membrane.

Discussion. Dr. A. L. Kornzweig asked about the various types of degeneration of the macula, and whether the pathology is the same.

Dr. Klien replied that the pathology was the same except for the appearance of Bruch's membrane. In angioid streaks the membrane stains black.

Ocular pathology in diabetes

Dr. Samuel Gartner said that diabetes is an important cause of visual impairment and blindness. The survival of more old people has increased the numbers suffering from this disease and insulin has prolonged their lives, so that we now see many more diabetics with eye lesions. The incidence of diabetic retinopathy increases with duration and severity of the disease regardless of the best modern care with diet and insulin, which does not prevent its onset and extension. A formula has been made to forecast the development of retinopathy.

Dr. Gartner described the pathology of diabetic retinopathy. There are hemorrhages, exudates, and cysts associated with extensive vascular damage.

All the cases examined showed some sclerosis of the arteries. Endothelial proliferation with canalization was found frequently in arteries and veins. Capillary disease was manifest by the formation of capillary aneurysms and capillary occlusions by endothelial proliferation. Rubeosis iridis probably follows the slow occlusion of the central retinal vein by phlebosclerosis.

Bernard Kronenberg,
Recording Secretary.

LOS ANGELES OPHTHALMOLOGICAL SOCIETY

September 2, 1948

DR. WILLIAM ENDRES, *chairman*

ALLERGY IN OPHTHALMOLOGY

Dr. Charles Petitt (by invitation) gave a comprehensive presentation of allergy as related to ophthalmology. The causes of inflammation are numerous and variable and depend on the rate of development of the reaction, its duration, and the release of substances such as histamine by the agent.

The histologic classification of lesions in allergy may be divided into two groups. The first necrotizing, in which there is some degree of necrosis. Parenchymal cells are present and eosinophilia is rare. Cincophen poisoning is an example of acute allergic necrosis. There may be either organ specificity or cell specificity such as anaphylaxis.

The second group are anaphylactoid or exudative reactions of which urticaria is an example. These are characterized by rapid onset, short course, and rapid regression. Secondary changes, as seen following any inflammation, are present. Cellular exudates, usually neutrophilic, are present but, if the condition is prolonged, eosinophilia predominates.

Eosinophilia is not pathognomonic of allergic states. Fibrinoid necrosis, which is focal and sharply delimited, such as periarteritis nodosa, may be present. This may or may not be on an allergic basis. Anaphylactoid reactions may follow injection of foreign serum. Rheumatic fever, which is a colloid disease, may be on an allergic basis since it is well known that the Ashoff nodule can be experimentally produced.

Granulomatous diseases in which tumor-like nodules are present are the result of inflammation. Examples of this are foreign-body reactions and sarcoidosis. There is no necrosis present in these conditions.

Allergic granulomas are characterized by central necrosis. These may be divided into two types: (1) The tuberculoid group which is caused by well-known agents such as tuberculosis, tularemia, mycosis, and brucellosis. These show positive skin tests to the causative agent. (2) Rheumatoid diseases of which there is no known etiology or positive skin test. Most rheumatoid diseases can be experimentally produced.

In vernal catarrh the diagnostic criteria are plaques in the conjunctiva especially superiorly. These plaques are usually pale and are not red and injected. The fornix is not usually involved and, on section, lymphocytic and fibrous tissue are seen. Eosinophilia are present in conjunctival secretions and the bacteriologic findings are the usual conjunctival inhabitants.

The disease follows a seasonal incidence usually occurring in the warm months—more often in children and especially boys. It is interesting to note that the seasonal incidence does not correspond with the seasonal incidence of pollens. Food sensitization has not been established and the picture, histologically, is not consistent with allergic manifestations. These patients rarely show positive skin tests and there is no greater incident in allergic than in nonallergic individuals.

The speaker did not believe that vernal catarrh is due to allergy nor did he believe that it was due to infection. Vaccine therapy has been of no help whatever. There are many types of conjunctivitis which are allergic and are due to dust, yeast, foods, and so forth.

In treatment, radium will alter the inflammatory states. If the allergen is given properly, a desensitization usually occurs and the condition is at least temporarily controlled.

Daniel B. Esterly,
Secretary.

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Author's proofs should be corrected and returned within forty-eight hours to the *Manuscript Editor, Mrs. Katherine F. Chalkley, Lake Geneva, Wisconsin.* Twenty-five reprints of each article will be supplied to the author without charge. Additional reprints may be obtained from the printer, the George Banta Publishing Company, 450-458 Ahnaip Street, Menasha, Wisconsin, if ordered at the time proofs are returned. But reprints to contain colored plates must be ordered when the article is accepted.

ELECTROPHYSIOLOGY

In 1849, Emil du Bois-Reymond placed the anterior and posterior poles of a vertebrate eye between two electrodes connected to a galvanometer and found that, independent of illumination, a current passed from the cornea to the fundus of the order of 6 millivolts. Since this demonstration of an electrical response from the eye, a century of zealous study has been devoted to the phenomenon.

Du Bois-Reymond, although of Swiss-French extraction, was born and educated in Berlin. Like his fast friend, Helmholtz, he was inspired by the illustrious teacher, Johannes Müller. Humbolt, in 1841, read a report of some simple experiments in animal electricity and suggested to Müller exploration of this field. Müller handed the problem to du Bois-Reymond, whose investigations continued for the next 40 years. After seven years, then aged 30 years, he published the first of his celebrated volumes on "Researches in Animal Electricity." At the death of Müller, 10 years later, he was awarded the Chair of Physiology at the University of Berlin.

The action current of the retina, now

called the electroretinogram, was discovered in 1866 by Holmgren, and simultaneously by Dewar and McKendrick of Scotland whose paper was actually in print when Holmgren's article was published. The Scotch investigators later observed, in 1873, that the invertebrate eye with its erect retina has a resting potential of the opposite sign to that of the vertebrate eye, signifying that the electric response of the eye, at rest as well as in action, is maintained by the visual cells.

The sensitive capillary electrometer enabled the Englishman Gotch to obtain, in 1904, the first electroretinogram that embodied all the features now known. The technique of valve amplification, which is now standard practice, was introduced by the Americans, Chaffee, Bovie, and Hampson, in 1923, and the retina was the first sense organ to be thus studied. By its means, Adrian demonstrated, in 1928, that an optic-nerve fiber responds to increased stimulus by increased rate of discharge, the size of the impulse remaining constant.

The analysis of the polyphasic response of the retina to light was initiated by Granit in 1932. His experiments with selectively acting agents proved that the vertebrate electroretinogram is built from at least three distinguishable components.

In 1938, Hartline isolated single fibers of a vertebrate optic nerve and demonstrated that all do not respond to light in the same way, and that a large number of visual units evidently respond only to changes in intensity. Shortly thereafter, Granit advanced Hartline's work by placing micro-electrodes directly on the retina, and so determined the color sensitivity of small groups of retinal elements—experiments which resulted in his modulator-dominator theory of color vision.

The electroretinogram affords a sensitive objective expression for the effects of light upon the retina. Even the luminosity curve is quantitatively reflected by the electrical response, as Granit revealed in 1943.

Among the contributors to the study of human electroretinograms are Karpe of Sweden, Spellberg of Russia, Amsler of Switzerland, and Adrian of England. Adrian has been his own subject in most of his work, operating the instruments by strings led into the dark room. The clinical application is illustrated by a case of Amsler's with variable concentric contraction of the visual field following trauma. Since the electric responses corresponded to a normal field he concluded that the contraction was due to a functional block at the cortical level.

The variation of the resting potential that occurs in the eye movements of reading can be recorded through electrodes placed at the external canthus of each eye. The graph closely duplicates the photographic record, but the electro-oculogram has the advantage of requiring no restraint nor the presence of a glare light. This method, perfected by Miles in 1939, was recently utilized by Carmichael and Dearborn in the most comprehensive study of reading and visual fatigue yet made. James E. Lebensohn.

THE FRENCH OPHTHALMOLOGICAL SOCIETY

The French Ophthalmological Society opened its 56th annual congress in 2,000-year-old Paris, at 8:30 a.m., on Sunday, May 22, 1949. The meeting lasted the customary six days. The mornings were devoted to papers and discussions and the afternoons to visiting hospitals.

Some 400 members attended, out of a total membership of 1,200. Strange to say, the French are far in the minority, numbering only 500, the other 700 members being foreigners. It is never possible for all to be present at any one meeting.

Twenty-three countries were represented: France, England, Ireland, Belgium, Switzerland, Italy, Holland, Spain, Portugal, Yugoslavia, Turkey, Greece, Syria, Lebanon, Iran, Poland, Denmark, Sweden, Luxemburg, United States, Colombia, Brazil, Argentina, and the town of Gibraltar.

The symposium of the congress, on uveitis with hypertension, was opened by Marcel Kalt. The discussers were J. François who spoke on gonioscopy in hypertensive uveitis; J. D. Blum and S. Forni on results of cyclodiathermy coagulation on the surface in secondary hypertensions; Hambresin on what collyria should be employed in hypertensive uveitis; Florian Verry on the aqueous humor in the hypertensive syndrome of uveitis; and Nectoux on the action of metamethylarmine (M.M.P.) on the eye and its employment in hypertensive uveitis.

The masterly review of the entire subject by Kalt and the gracious manner in which he replied to the discussers created a most favorable impression.

J. Q. Barraquer read a paper on postoperative complications of keratoplasty and Arruga one on the mechanical role played by retrobulbar injection in operations for strabismus. (It was during the meeting that Arruga was awarded the Gonin medal by the International Council of Ophthalmology then in session in Paris.) Valiere-Vialeux's paper on liquefaction of the vitreous and the loss of it in cataract extraction causing collapse of the globe was particularly instructive. Kirby's demonstration (using films and projection) of his technique for intracapsular extraction was excellent.

In the more than 60 presentations, almost every field of ophthalmology was touched on, surgery predominating. The proceedings were so efficiently conducted that no precious moment was lost. As a rule each discusser was already on the steps to the platform or actually on it before the speaker had concluded his last sentence. Nothing could be more stimulating and educational than to attend a session of the French Ophthalmological Society.

For the afternoons some 15 hospitals had prepared special operative and clinical programs which had all been posted the first day of the congress.

All through the week, in a large room under the meeting hall, there was held an exhibit, surprisingly fine for the times, of surgical instruments and various appliances gathered from many countries of Europe.

The afternoon for the traditional outing in the country fell on the third day. This time it was by bus to Malmaison and its lovely gardens, so reminiscent of the glorious days of the Consulate and the sad hours of the Emperor's abdication. On the way back to Paris a rarely enjoyable hour was passed in Villenes at Dr. Gabriel Renard's country place, hidden away from the roadside, in its lovely grounds, by trees and shrubs.

The banquet took place in the evening. Two hundred and eighty-two guests sat down at table. Paris still shows scars from bullets and fires of the recent conflict, especially around the Place de la Concorde, but gastronomically the recovery has been complete, as was borne out by the delicious dinner and the food everywhere. Prendront la parole à la fin du diner, the president of the banquet, Sir Stewart Duke-Elder, made a most appropriate speech, as did Dr. Appelmans, Dr. Alvara, Dr. Streiff, and Dr. Rossi who sat at his table. The secretary general, Dr. Edward Hartmann, on whose shoulders had fallen the brunt of the whole congress, replied in the name of the society. His speech was on a very felicitous note that brought into the scene, one by one, each country that was represented.

Concerning the beginning of an organization that has met with well-nigh unprecedented success and world renown it will be informative to turn the pages of ophthalmology back to the year 1857 when the first International Ophthalmological Congress was held. Because it met at long intervals and at great distances and because the evolution of ophthalmology was proceeding so rapidly, the desirability of forming national societies for more convenient discussions arose which in turn have led to local societies. The German Ophthalmological Society of Heidelberg came into existence in

1863, the American Ophthalmological Society in 1865 and the Ophthalmological Society of the United Kingdom in 1880. The French Ophthalmological Society, at its foundation in 1883, was patterned after the Heidelberg society. However, it was to be an organization composed exclusively of French-speaking oculists. The Germans, when they heard of the new society, in sending their congratulations, made it known that, although their mother tongue was different from the Latin, they nevertheless hoped that the French would extend to them the hospitality of their meetings.

The granting of this desire was destined to have a far-reaching effect. At the second congress, in 1884, no less personages than Art and Hirschberg of Berlin, Bowman of London, Becker of Heidelberg, Donders of Utrecht, Horner of Zurich, Pflüger of Berne, and Reymond of Turin were numbered among the 112 members present. Today, among those from afar, are 21 members from the United States.

The society, like so many others, is but the lengthening shadow of one man, Chibret, of Clermont-Ferrand, whose initiative created it and who sent out the call for its first meeting. It always sits in Paris. Only twice has it gone elsewhere. In 1923, it met in Strasbourg at the centenary of Pasteur and, in 1925, in Brussels where at its opening session it was honored by the presence of her Majesty the Queen.

The society is governed by a committee of 12—5 members from Paris, 6 from the French provinces, and 1 from a foreign country. There is no president but instead a secretary general. It is often called the most international of all the national societies. Bernard Samuels.

ACTA OPHTALMOLOGICA POLONICA

A Polish journal of ophthalmology has been launched. It is a quarterly publication called *Klinika Oczna, Acta Ophtalmologica Polonica,* and is a most promising journal. The paper is not nearly so good as that which we use and the half tones, although adequate, are certainly less crisp than they might be. But the intellectual content, on the other hand, has great merit. The scholarly articles in Polish are also presented in a very extensive abstract in English or French. The first articles in the first of the two issues that have been received report the work of Wilczek Marian on the lamina cribrosa which also appeared in the *British Journal of Ophthalmology.* There are also articles on refraction, physiologic optics, glaucoma, streptococcus, and on lesions of the cornea and retina.

The new journal is a welcome addition to ophthalmologic literature. We congratulate our Polish colleagues and wish them success in this fine venture. F. H. Haessler.

OBITUARIES

ROBERT J. CURDY

(1868-1948)

Robert J. Curdy was born January 25, 1868, at Humbolt, Kansas. He was the son of William Wilson Curdy and Helen Sackett Curdy. There were two brothers and one sister. He received his early education in the public schools of Humbolt, Kansas, and then attended the College of Liberal Arts and Sciences at the University of Kansas, 1883 to 1886. He received the degree of Doctor of Medicine from Washington University in 1895, and completed the postgraduate course in 1896 (cum laude). He then entered the office of Dr. John Green, Sr., and was his assistant for three years. The following year he spent in study and in working in several leading European clinics. On his return to the states, Dr. Curdy opened his office in Kansas City, Missouri, for the practice of ophthalmology and remained in active practice to the day of his death, December 15, 1948.

Dr. Curdy became a member of the

American Ophthalmological Society in 1906 and was made emeritus member in 1938. He was a past president of the Kansas City Society of Ophthalmology and Otolaryngology. He was also a fellow of the American College of Surgeons and the American Academy of Ophthalmology and Otolaryngology. He was a member of the staffs of St. Luke's, Research, Municipal, St. Margaret's, and Children's Mercy Hospital and remained active in the clinic of the latter until 1946.

Dr. Curdy published many scientific articles and was the first to advocate equal recession and resection in horizontal strabismus. He was also first to advocate the external approach in narrow-angle glaucoma, and designed a special knife for the purpose of performing the Lagrange sclerectomy by the external approach.

He was married to Ann Richardson Hall on November 3, 1906. Two daughters, Helen and Isabel, and Mrs. Curdy, survive.

Robert Curdy was a keen clinician and was unsurpassed in presenting and discussing the differential diagnosis in an obscure case. He was one of those rare individuals who knew no enemies, either in or out of the profession, and never once was he known to have said an unkind word of anyone. Robert Curdy has died but his memory and ideals will live on in the minds of us who have been privileged to have known him intimately. Albert N. Lemoine.

DAVID L. TILDERQUIST
(1872-1948)

With the passing of David Tilderquist on September 26, 1948, the medical profession lost one of its most unassuming but devoted ophthalmologists and the people of the Northwest lost a well-beloved friend and skilled physician, who had served them for 44 of his 76 years. Dr. Tilderquist will always be remembered for his humble and kindly manner, his generosity, his unswerving loyalty to all that was good, and for an integrity of character which endeared him to everyone who knew him.

He was born in Vasa (Goodhue County), Minnesota, on October 22, 1872. He lived and worked on the parental farm, attending the local public schools and then Gustavus Adolphus College in St. Peter, from which institution he was graduated in 1894. After teaching in the public and parochial schools in Goodhue County and at Hope Academy in Moorehead, Minnesota, for six years, he entered the University of Minnesota with a keen desire to become a chemist. His brother, William, a mining engineer, prevailed upon him to continue his studies in medicine rather than chemistry and, in 1903, after he was graduated from the University of Minnesota, he spent a year interning at Swedish Hospital in Minneapolis—in the days when many medical students entered practice without benefit of internship. Dr. Tilderquist spent much time in the pathologic laboratory doing independent study.

He established a general practice in Duluth, in 1904, which, from the early days, taxed even his great capacity for long hours of work. He studied abroad first from 1910 to 1911, when he specialized in ophthalmology and otolaryngology, and then again in 1924, when he took further work in Vienna.

Dr. Tilderquist held a number of hospital staff appointments during his long years of service in Duluth, including that of chief of staff at St. Luke's Hospital, and chief of the Eye, Ear, Nose, and Throat Service at St. Mary's Hospital. During the past 25 years he had taught the nurses' classes in ophthalmology at St. Luke's Hospital and annually offered awards for scholarship in therapy and bedside nursing. He was instrumental in establishing and running the ophthalmologic service of the Methodist Dispensary for many years and later assumed more than his share in the ophthalmic work of the Miller Memorial Hospital Dispensary, when younger men were not available to carry on the service.

In 1926, Dr. Tilderquist was president of the Minnesota Academy of Ophthalmology and Otolaryngology; at the time of his death he was serving as its vice-president. He was a member of the American Academy of Ophthalmology and Otolaryngology, a member of the American Medical Association, the American College of Surgeons, the Minnesota State Medical Association, and the St. Louis County Medical Society. He was a diplomate of the American Board of Ophthalmology and the American Board of Otolaryngology.

He was an ardent student and followed the ophthalmic literature closely. His mind was a scholarly one and his reading was not aimless. In addition to following the current literature, he always pursued one or more definite lines of study. He wrote few articles, largely because of his extreme modesty. For many years he found time to abstract Scandinavian ophthalmic literature for the AMERICAN JOURNAL OF OPHTHALMOLOGY, whose editor was his close friend, Edward Jackson. He developed a few surgical instruments, which are on the market, but of which he never spoke.

This quiet scholar encouraged studious habits in others; his was the moving spirit in the small local organization of ophthalmologists and he it was who stimulated the members to study and to make reports. He always faithfully attended the meetings of the local county society, the weekly pathologic conference, the Minnesota Academy of Ophthalmology, and the American Academy of Ophthalmology. He was always most kindly and generous to younger men, several of whom, it has been learned, he helped through medical school. He established a scholarship at his alma mater, Gustavus Adolphus, for freshmen who give promise in scientific study. In 1946, this college honored him with a special award as one of the outstanding alumni who had been of great service.

His generosity and unselfishness are typified in the letter, accompanying a research grant given to the writer, which reads in part:

"Enclosed herewith please find a gift in the interest of research. . . . You may use this fund in any way you see fit, or you may even reimburse yourself from it for expenses incurred or for losses sustained or compensate yourself for time spent on account of research done in the past.

"This fund is meant to be a help and not a burden. Therefore it does not carry with it the implication that any research must be carried out that would not otherwise have been undertaken without the fund.

"Wishing you many dividends in the form of new knowledge and much enjoyment and satisfaction. . . ."

Dr. Tilderquist gave unstintingly of himself to his patients; no matter how late the hour or how great his own fatigue, he worked patiently and carefully with each one. Colleagues, who sought his consultations frequently, did so because they felt assured an exhaustive and conscientious study would follow.

Dr. Tilderquist had the rare good fortune to experience, while he was still alive, hundreds of expressions of love and admiration, which so often go unsaid. His measure, indeed, was overflowing with the admiration, respect, and love of his colleagues and his thousands of grateful patients and friends.

A. C. Hilding.

CORRESPONDENCE

BETA IRRADIATION OF THE EYE

Editor,
American Journal of Ophthalmology:

In a recent pamphlet distributed by Dr. Harold Swanberg describing his radium-D applicator, produced by the Canadian Radium and Uranium Corporation, quotations were made from the article by Hughes and Iliff, "Beta irradiation of the eye," AMERICAN JOURNAL OF OPHTHALMOLOGY, 32:351 (March) 1949.

The results of beta radiation reported in

this article were obtained by using radon (not radium-D) applicators. The experiments and clinical results from the use of a Swanberg radium-D applicator at the University of Illinois have been reported by Dr. Fred M. Wilson at the 1949 meeting of the Association for Research in Ophthalmology.

Dr. Wilson found important differences between the effects of radium D and radon, the former showing about 40-percent effective beta output and less penetrating power. These differences are important in the practical aspects of treatment; for example, duration of treatment and ability to eliminate corneal vascularization and other pathologic processes situated more deeply in the lids, cornea, and sclera.

(Signed) William F. Hughes, Jr.,
Chicago, Illinois.

Staining technique for trachoma inclusions

Editor,
American Journal of Ophthalmology:

In the May, 1949, issue of the Journal, page 702, Lieut. V. O. Eareckson brings forward Wright's staining method as "a rapid staining technique for the demonstration of trachoma inclusions." Forty years ago I brought forward the same method for the same purpose—"A rapid method of staining the trachoma bodies of Halberstaedter and Prowazek," *Ophthalmic Record*, October, 1909. Probably the reason it did not come into general use was that it requires more careful attention to detail than does the Giemsa method.

(Signed) F. H. Verhoeff,
Boston, Massachusetts.

BOOK REVIEWS

Toxic Eye Hazards. A manual prepared by the Joint Committee on Industrial Ophthalmology of the A.M.A. and the American Academy of Ophthalmology and Otolaryngology. Publication No. 494. New York, The National Society for the Prevention of Blindness, 1949. 34 pages, 10 illustrations, bibliography. Price, $1.00.

The preparation of this manual and the extensive work that went into its background excites profound admiration for all who had a part in its formation and assisted in its publication.

It is a factual, practical, and inexpensive masterpiece of great use to industry and ophthalmologists working with industrial eye problems.

Chapter I has to do with standards and tests for eye-protection equipment. It describes, as an example, a well-organized eye-protection program. Part II of the first chapter gives tables of toxic compounds and the ocular signs and symptoms they produced.

Chapter III contains an excellent description of standard emergency and first-aid procedures in chemical eye injuries, based upon the completely satisfactory results obtained from practical experience.

The manual should be read and studied by every ophthalmologist, whether interested in industrial ophthalmology or not, and by every physician employed by industry. Derrick Vail.

Ueber wertung angeborener Fehler des Farbensehens. By Georg Wilhelm Keyser, M.D. Oslo, Norway, A. W. Brøgger Press, 1943. Paper covers. 174 pages, bibliography, 2 colored plates. Price, not listed.

The problems of color vision have excited a marked recrudescence of interest in the past decade. Keyser, as a practicing ophthalmologist, is primarily concerned with the color capacity requisite for the performance of various tasks. The introductory chapters review both critically and comprehensively the contributions to our knowledge of color deficiency, from the original discovery by Dalton of his own color blindness in 1794 to the present.

Then follows a detailed analysis of the signals used in railroading, navigation, aviation, and military maneuvers. Keyser objects to the Nagel anomaloscope because it tests only foveal function, whereas he maintains that the parafoveal area, because of irradiation and dispersion, should be of principal importance in signal discrimination.

Keyser prepared a strip of color film that recorded a blinking red light in Oslo harbor. With this strip he tested men from 11 to 77 years of age, classified by the standard tests as normal or having various types and degrees of color deficiency. Only deuteranopes failed consistently in the test, calling the red light green. The anomalous trichromats named the color correctly.

He asserts that modern signal devices largely eliminate the danger of wrong interpretation by the color deficient. However, he would consider any form of color weakness as a serious handicap in medical practice, as the undue color contrast characteristic of anomalous trichromats may induce false judgments on tissues and bacterial slides.

The book is highly stimulating and suggests the need of further studies on the practical problems of color deficiency in connection with the conditions of the assigned tasks. It is to be hoped that Keyser will soon complete the English version of this work according to his original intention.

James E. Lebensohn.

How to Become a Doctor. By George R. Moon, A.B., M.A. Philadelphia, The Blakiston Company, 1949. 130 pages. Price, $2.00.

The boy or girl interested in a medical career is often at a loss for where to turn for advice on where to go for his medical education, for information about the courses given, and how to qualify to take them.

Moon has performed a much-needed task in giving this information in a compact form that is highly successful in its aims. It is a "complete guide to the study of medicine, dentistry, pharmacy, veterinary medicine, occupational therapy, chiropody and foot surgery, optometry, hospital administration, medical illustration, and the sciences."

It should be in the hands of anyone who is preparing to "become a doctor."

Derrick Vail.

Gli Antibiotici in Oftalmologia. By Antonio Grignolo. Torino, Minerva Medico Press. 321 pages, 21 figures. Price, not listed.

This thorough monographic treatment of the antibiotics is to be highly recommended to Italian readers. The author has not favored us with summaries in another European language, as have some of his countrymen, but it is arrogant to expect this from one who writes in a language which was used by perhaps the only poet who is the equal of Shakespeare. The date of publication is not stated but the bibliography contains reference to publications in 1948.

The entire subject is adequately treated. After a brief introductory statement on the nature of the antibiotics, the work on penicillin and streptomycin is extensively described and many other antibiotics are given shorter but adequate review. The preparation, titration, biologic properties, tolerance, and dosage are discussed from personal experience and on the basis of a thorough review of the literature.

Even more extensive treatment is accorded the specifically ophthalmic experience. Diseases of each ocular tissue are discussed in detail and the merits, as well as inadequacies, of antibiotic therapy are evaluated. Each section has an extensive list of references. F. H. Haessler.

ABSTRACT DEPARTMENT

EDITED BY DR. F. HERBERT HAESSLER

Abstracts are classified under the divisions listed below. It must be remembered that any given paper may belong to several divisions of ophthalmology, although here it is mentioned only in one. Not all of the headings will necessarily be found in any one issue of the Journal.

CLASSIFICATION

1. Anatomy, embryology, and comparative ophthalmology
2. General pathology, bacteriology, immunology
3. Vegetative physiology, biochemistry, pharmacology, toxicology
4. Physiologic optics, refraction, color vision
5. Diagnosis and therapy
6. Ocular motility
7. Conjunctiva, cornea, sclera
8. Uvea, sympathetic disease, aqueous
9. Glaucoma and ocular tension
10. Crystalline lens
11. Retina and vitreous
12. Optic nerve and chiasm
13. Neuro-ophthalmology
14. Eyeball, orbit, sinuses
15. Eyelids, lacrimal apparatus
16. Tumors
17. Injuries
18. Systemic disease and parasites
19. Congenital deformities, heredity
20. Hygiene, sociology, education, and history

2

GENERAL PATHOLOGY, BACTERIOLOGY, IMMUNOLOGY

Buschke, W. **Morphologic changes in cells of corneal epithelium in wound healing.** Arch. Ophth. **41**:306-316, March, 1949.

The authors report their experiments with corneal injuries in rats and frogs. Pseudopodial extensions of the cytoplasm directed into the denuded area are seen in the basal layers of the epithelium in the early stages of healing of pinprick injuries. These pseudopods are observed particularly in pockets of the wound margin during the healing of larger injuries. Spreading and flattening of the epithelial cells, which lead to sealing off of the wound margin, occur in linear and larger lesions in the early stages. This sealing off is seen also in the healing of small injuries in the superficial layers of the epithelium. Ralph W. Danielson.

3

VEGETATIVE PHYSIOLOGY, BIOCHEMISTRY, PHARMACOLOGY, TOXICOLOGY

Agrest, A., Roncoroni, A. J., García Badaracco, J. E., and Vidal, F. **Carbaminoylcholine in rabbits with partial parathyroidectomy.** Arch. de oft. de Buenos Aires **23**:294-297, Oct., 1948.

The authors feel that the tetany of hypoparathyroid states occurs because the hypocalcemia modifies the sensitivity of acetylcholine. Partial parathyroidectomy was performed on rabbits and carbaminoylcholine was used as an index of the activity of acetylcholine. In some hypocalcemic animals observed, the ocular tension did rise as the body contractions increased, and when calcium was administered intravenously the tetany diminished and the tension was lowered. However, as yet, it is not possible to draw any satisfactory conclusions. (4 graphs.) Edward Saskin.

Baumann, Adamo. **First report on experimental researches in electroretinography.** Ann. di ottal. e clin. ocul. **74**:375-380, May, 1948.

A suitable subject for electroretinography was found in a woman with craniofacial dysostosis whose eyeball could be dislocated so far forward that an electrode could be applied to the posterior pole of the globe. Baumann found that as the intensity of the luminous

stimulus is increased the retinal action current likewise increases up to a point beyond which further increase in the stimulus results in decrease in the action current. (References.)

Harry K. Messenger.

Cristini, G., **The vascular action of pilocarpine, eserine, adrenalin and atropine, and their influence in primary chronic glaucoma.** Brit. J. Ophth. **33**:228-242, April, 1949.

Pilocarpine and eserine do not dilate the large vessels of the iris and ciliary body but dilate the capillary bed and open new capillary districts. Although this produces an increase of the sum of resistances in the circulation, the total result is reduction of the mean capillary hydrostatic pressure and, therefore, of the ocular tension. Atropine dilates the large vessels, but does not open new capillary beds. This decreases the sum of resistances and, therefore, increases the mean hydrostatic pressure whenever the capillary bed is already impaired, as in chronic glaucoma. Adrenalin dilates both the large vessels and the capillaries and increases the circulatory bed. The result is an increase in the sum of resistances, and a decrease of the mean capillary hydrostatic pressure and of ocular tension. In acute glaucoma, however, the excessive permeability in the capillaries for plasma proteins may produce elevation of intraocular pressure. Orwyn H. Ellis.

4

PHYSIOLOGIC OPTICS, REFRACTION, COLOR VISION

Swan, K. C. **Pharmacology and toxicology of the cornea.** Arch. Ophth. **41**:253-275, March, 1949.

This article combines literature, original research, and practical suggestions in therapy so admirably that it should be read in full. R. W. Danielson.

Vidal, F., García Badaracco, J., Agrest, A., and Roncoroni, A. J. **Neurocapillary test in rabbits.** Arch de oft. de Buenos Aires **23**:292-293, Oct., 1948.

Carbaminoylcholine solution, 0.33 percent, was instilled into rabbits' eyes with these results: increased lacrymal and salivary secretion within three minutes, increased intestinal motility and diarrhea within five minutes, increased pulse rate, conjunctival vasodilatation, and miosis. Influence on ocular tension was equivocal. (2 graphs.) Edward Saskin.

Woods, A. C. **Experimental studies on the pathogenesis and treatment of ocular tuberculosis.** Brit. J. Ophth. **33**:197-228, April, 1949.

The author reports on 12 years of investigation in which human strains of the tubercle bacillus were injected into the anterior chamber of rabbits. In the study of pathogenesis the influence of the number and virulence of organisms was determined. Small doses of virulent bacilli in a normal animal produce a slowly-spreading infection. A larger dose accelerates the reaction. In the immune-allergic rabbit the propagation and spread of the organisms is restrained. With a large dose the immunity is overwhelmed and the animals develop an acute destructive inflammation. In both the normal and immune-allergic animals the ocular inflammation resulting from infection approximates the degree of ocular sensitivity. Desensitization before inoculation abolishes the primary ocular reaction to tuberculoprotein, and the ocular inflammation is of low degree when the desensitization is maintained. The resistance to reinoculation was totally undisturbed by complete densensitization before inoculation. With high cutaneous sensitivity the ocular sensitivity is also high; however, ocular disease may produce great ocular sensitivity without affecting a normally low cutaneous sensitivity. The transient

immunity to re-inoculation shown by eyes that have recently recovered from tuberculosis is due to the presence of persisting macrophagic cells. Desensitization with tuberculin is accompanied by a marked decrease in manifestations of the disease. It removes the destructive factor. If tuberculin treatment is stopped the tissue sensitivity, and in many animals the ocular lesion, recur. The relatively nontoxic sulphone, promizole, has a deterrent action on the local tuberculous lesion in the immune-allergic rabbit, and when combined with streptomycin eradicates the bacilli from the infected tissue of most of the animals, and curtails their growth and virulence in the others.

Orwyn H. Ellis.

5

DIAGNOSIS AND THERAPY

Bunge, E. **A new method for quick determination of the dominating eye.** Klin. Monatsbl. f. Augenh. **114**:69-71, 1949.

An observer looking into two mirrors joined by a stick at a right angle will note double images. The image in the dominating eye is the more disturbing. The author discusses his method and compares it with others. Max Hirschfelder.

Dattner, B., Distelheim, I. H., and Maltzer, L. **BAL in arsenical optic neuritis.** New York State J. M. **49**:190-192, Jan. 15, 1949.

BAL has been found to be of value in removing arsenicals and heavy metals from living tissue. Pentavalent arsenic was used for pemphigus vulgaris and toxic optic neuritis secondary to the treatment was relieved by the intramuscular use of BAL. The dosage used was 0.5 cc. intramuscularly, increased by 0.5 cc. every three hours until 2 cc. is reached. Ephedrine sulphate 0.24 gm. is given orally one half hour before each dose and at the time of injection of BAL it is repeated. BAL must be used with caution. It produced a toxic psychosis in this patient during the course of treatment.

H. Weinberg.

García Notico, F. **New technique for the inclusion of muscles on a spike, in enucleations.** Arch. de oft. de Buenos Aires **23**:216-219, Sept., 1948.

The plastic prosthesis has a central cone behind, which extends back into the muscle cone. The anterior portion consists of a hemisphere, from which a spike projects forward. Near the circumference are four slits, through which the muscles are drawn forward and impaled on the spike. They are then sutured together. Tenon's capsule is sutured over the muscle ends, and the conjunctival covering is closed. A conformer is placed in the conjunctival sac, which has a hole in the center to receive the tip of the spike. Iced compresses are used during the first twenty-four hours and pressure bandages for five days. A. G. Wilde.

Goldman, H. **Slit-lamp examination of the vitreous and the fundus.** Brit. J. Ophth. **33**:242-247, April, 1949.

Inflammations, detachments, cysts, degenerations and tumors can usually be definitely diagnosed by fundus biomicroscopy, with the help of a fundus lens and the author's own prism for reducing the angle between the illuminating beam and the corneal microscope.

Orwyn H. Ellis.

Jaeger, A. **An addition to the nyctometer of Comberg.** Klin. Monatsbl. f. Augenh. **114**:82-84, 1949.

In order to avoid variation in illumination of the Comberg nyctometer it is necessary to test the incandescent lamp more exactly than is possible by the use of a simple ampere or volt meter. The author describes a photometer for this purpose. (1 figure.) Max Hirschfelder.

Toennis, W. **Indications for surgical treatment of tumors in the sella turcica.** Klin. Monatsbl. f. Augenh. **114**:1-18, 1949.

In a postgraduate lecture the author surveys tumors in the region of the sella turcica, which are about one fifth of all intracranial tumors. The pathologic findings associated with various tumors of this region (pituitary tumors, craniopharyngiomas, meningiomas, gliomas, aneurysm, epidermoids, arachnoiditis, tumors of the cranial base) are discussed briefly. (9 figures, references.)

Max Hirschfelder.

6
OCULAR MOTILITY

Abbate, Vincenzo. **A case of paresis of the elevator of the left upper lid and of the left external rectus, treated with injections of irradiated maternal blood.** Ann. di ottal. e clin. ocul. **74**:369-374, May, 1948.

The nine-year-old patient received daily for eight days an injection of 4 cc. of her mother's blood which had been exposed for five minutes to ultraviolet radiation. Complete recovery ensued in about three weeks. The efficacy of irradiated maternal blood is ascribed not only to its physical properties but also to imponderable spiritual factors which transferred only from a mother to her child.

Harry K. Messenger.

Bruens, E. **Sutures used in resection for strabismus.** Klin. Monatsbl. f. Augenh. **114**:62-69, 1949.

The author describes a modification of Blaskovics' two U-shaped sutures for his resection. (20 figures, references.)

Max Hirschfelder.

Bursaux, M. O. **Orthoptic treatment for strabismus.** Ann. d'ocul. **182**:128-132, Feb., 1949.

The author compares the newer principles, methods and instruments used in orthoptic treatment with those of the older French masters such as Javal, Remy and Landolt. Several French ophthalmologists studied orthoptics in the United States and Great Britain during and after the war. In their writings they have introduced the newer instruments, methods and principles to French ophthalmologists. An orthoptic clinic has been established in the Lariboissiere Hospital in Paris. The newer methods are but slightly improved adaptations of the fundamentals laid down largely by French ophthalmologists several generations ago. In many cases the results have been no better than those obtained with the older orthoptic methods.

Chas. A. Bahn.

Gartner, S., and Billet, E. **Progressive muscular dystrophy involving the extraocular muscles.** Arch. Ophth. **41**:334-340, March, 1949.

A lesion of the nerve supply is so commonly the cause of palsy of an extraocular muscle that there is a great tendency to forget the rarer occurrence of a primary muscular disorder. Progressive muscular dystrophy was the cause of ptosis and divergent squint in a case presented. This case is the second in which histologic study of the extraocular muscles has been reported and the first in which involvement of the extraocular muscles has been demonstrated in a case of generalized progressive muscular dystrophy. The differentiation of primary muscular dystrophy and secondary muscular atrophy is discussed.

Ralph W. Danielson.

Gasteiger, H. **Some rarely performed muscle operations.** Klin. Monatsbl. f. Augenh. **114**:49-54, 1949.

In four patients a high degree of paralytic strabismus was corrected by the method of Vogt. Three had extreme convergence. The medial rectus was completely tenotomized and severed from all its connections. Double-armed sutures were then laid through the superior and

through the inferior rectus and conducted laterally, subconjunctivally, and through the skin to a point lateral to the outer canthus. They pulled the eyeball straight and were removed after ten days. A similar method was used for a contraction of the superior rectus in the fourth patient. Muscle transplantation was done in three patients with paralytic strabismus. This method is of advantage when strong secondary contracture of the antagonist is lacking. (9 figures, references.)

Max Hirschfelder.

Kunz, E. **A method for exact dosage of strabismus surgery.** Klin. Monatsbl. f. Augenh. **114**:55-62, 1949.

The effect of surgery in horizontal strabismus is mathematically analyzed. The rotation of the eye after unilateral surgery corresponds to the actual amount of advancement or recession multiplied by an undetermined factor. This factor is a fraction, the numerator of which is the elastic power of the antagonist, and the elastic powers of both muscles is the denominator. If equal amounts of recession and advancement are done on the two horizontal muscles at the same time, this factor can be disregarded. The article shows mathematically why this is the case. A schedule indicating the necessary amounts of recession and resection for all degrees of horizontal strabismus is displayed. (References.)

Max Hirschfelder.

Lienau, R., and Alvarez Montalván, E. **Bilateral congenital paralysis of the facial muscles and the lateral rotators.** Arch. de oft. de Buenos Aires **23**:272-275, Oct., 1948.

A 20-year-old man was unable, from birth, to move his eyes outward, had bilateral facial paralysis, and a deformity of the feet. He had a moderate loss of visual acuity and normal fundi. The oculomotor apparatus was defective in associated lateral version. He could converge and at times force a bilateral diversion. There was only elementary fusion. (13 figures.)

Edward Saskin.

Loutfallah, M. **Surgery of the inferior oblique.** Ann. d'ocul. **182**:81-121, Feb., 1949.

The muscles primarily and secondarily involved in paralyses of the vertical ocular rotation are discussed in detail. After a primary paralysis of the right superior rectus, a hyperfunction of the right inferior rectus and left inferior oblique may follow within a short time. Later a hyperfunction of the right inferior rectus and right inferior oblique with hypofunction of the left superior oblique may occur. The author presents the surgical anatomy and clinical physiology of the inferior oblique muscles at some length. Their proximity to the optic nerve and vorticose veins is important. Their torsional function is analysed. The indications for surgical weakening operations of the obliques include some forms of unilateral and bilateral hypophorias and tropias which may primarily involve the contralateral superior rectus; also disassociated vertical deviations with or without faulty insertion of the internal rectus. Methods for weakening include recession (White), myectomy with lid incision (Bonnet) and with conjunctival incision (Parker). Strengthening or reinforcing procedures include: resection (Berens), tucking (White), and advancement (Wheeler). Transplantation of the inferior oblique (Weiner) is seldom considered of value. Among the contraindications to inferior oblique surgery are slight and transient disassociated deviations, and faulty insertions. Operations and postoperative complications are discussed. Finally, an analysis of 38 operations performed by the author is presented in detail. The author prefers recessions and resections near the sclera to myectomy. (52 references.)

Chas. A. Bahn.

Piper, H. **The etiology of infantile ocular muscle disturbances.** Klin. Monatsbl. f. Augenh. **114**:42-49, 1949.

The author describes nine children who had strabismus with secondary underaction of certain muscles. The first of three groups comprises cases of concomitant squint, in which lack of function during an important stage of development led to an underaction of a muscle. The second group involves supranuclear disturbances. In the third group isolated muscle paralysis with degenerative changes (shortening) lead to an underaction of the antagonist. The retraction syndrome belongs in this group. (13 figures, references.) Max Hirschfelder.

7

CONJUNCTIVA, CORNEA, SCLERA

Appelbaum, H. B., and Hale, A. S. **Aureomycin in dendritic keratitis.** J. Michigan St. M. Soc. **48**:352, March, 1949.

The authors review the properties of aureomycin and its toxicity. A patient who had dendritic keratitis for over four years with frequent exacerbations was given two drops of aureomycin ophthalmic solution (0.5 percent) every two hours and was well in two days. There has been no recurrence. H. Weinberg.

Delaney, J. H. **Treatment of dendritic keratitis.** Pennsylvania M. J. **52**:845-847, Sept. 25, 1949.

Dendritic keratitis is caused by a virus. Iodine therapy is still the best method of treatment. Streptomycin seems to inhibit the progress of the virus and aureomycin may well be an effective drug.
F. H. Haessler.

Houet, R., and Weekers, R. **Xerophthalmia of the newborn and hepatic insufficiency.** Arch. d'opht. **9**:39-43, 1949.

The authors note that xerophthalmia in the newborn due to deficient intake of vitamin A is extremely rare, whereas xerophthalmia resulting from poor absorption of vitamin A due to various diseases, particularly of the intestinal tract, is more common. They describe two cases in which there was disturbance in the transformation of carotene into vitamin A in the liver. The first baby had a sudden attack of jaundice at the age of two months which recurred at intervals. At three months a corneal ulcer developed simultaneously with the onset of xerophthalmia. Following daily injections of 60,000 units of vitamin A, the xerophthalmia disappeared rapidly but the infant progressively lost weight and died. The lesion was a serious disturbance of the liver parenchyma. The second infant, premature at 7½ months, developed normally until the age of 3½ months when it developed bilateral corneal opacification with perforating ulcers of each eye. There appeared to be normal absorption of vitamin A and the diet had not been deficient. The child was placed on a daily dosage of 60,000 units of vitamin A and slowly improved, but the corneas healed with extensive scars.

The authors comment on the mechanism of vitamin A absorption and on the double role of the liver in vitamin A metabolism. It produces bile which emulsifies the fats, permitting absorption of vitamin A, and its parenchyma is concerned in the transformation of carotene into vitamin A. Phillips Thygeson.

Muller, P. **Mosaic degeneration of Bowman's membrane.** Ann d'ocul. **182**: 122-127, Feb., 1949.

This rare condition which Vogt has named "crocodile chagrain" is essentially a degeneration of Bowman's membrane which seems to be composed of round or polygonal cells. An illustrative case in a 51-year-old man is described. After slight injury to the left eye by a twig, hypopyon keratitis developed. Later, a transplantation operation was performed. The ex-

cised cornea showed breaks in Bowman's membrane, which were replaced by cicatricial tissue. Chas. A. Bahn.

Paraipan, C. **Severe corneal ulcer cured by intraocular penicillin in 48 hours.** Ann. d'ocul. **182**:133-134, Feb., 1949.

A 68-year-old man developed a severe corneal ulcer after injury. A solution of 10,000 units of penicillin to the cc. was injected into the anterior chamber and two subconjunctival injections of 10,000 units of penicillin were also made. The ultimate vision was 20/50.

Chas. A. Bahn.

Senà, J. A., and Cerboni, F. C. **Scleral excavations.** Arch. de oft. de Buenos Aires **23**:313-325, Oct., 1948.

After a discussion of the history and pathology of such common afflictions of the sclera as senile hyaline plaques, inflammatory processes, and scleromalacia perforans a case is presented in which there were bilateral excavations of the sclerae, temporally, with typical senile hyaline plaques. (8 figures, references.)

Edward Saskin.

Trovati, E. **The bacterial flora of the conjunctiva in certain exanthematous diseases of infancy.** Ann. di ottal. e clin. ocul. **74**:358-368, May, 1948.

The conjunctiva was not inflamed in scarlet fever and chickenpox; the conjunctival flora was normal in chickenpox, but in scarlet fever streptococci and staphylococci were isolated. Conjunctivitis is a usual accompaniment of measles, in which the flora is normal except for an increase in sarcinae, to which the conjunctivitis is attributed.

Harry K. Messenger.

Wenda, L. **The syndrome of blue sclerotics.** Arch. d'opht. **9**:44-47, 1949.

The syndrome is a constitutional one with numerous complications in different organs and tissues of the body although the principal manifestation is blue scleras. The blue coloration of the scleras is not due to pigmentation but to the thinness of the structures which reflects a disturbance of the tissues of mesenchymal origin throughout the body. The disturbance is particularly marked in the bones, and repeated fractures are the rule. The ligaments are the next most seriously involved and dislocations of the joints and prolapses of various organs are common. Hemorrhages are frequent due to faulty connective tissue in the blood vessels. Visual disturbances due to cataract and deafness due to otosclerosis are common. Myopia with staphyloma has been reported. Wenda reports two cases, one a young girl of 16 years, the other a woman of 60, both with the classical syndrome. He notes, however, that whereas cases of the complete syndrome are rare, many instances of the incomplete syndrome have been reported. He states that women are more subject to the syndrome than men and urges that persons with this disease marry only individuals who are strong and vigorous.

Phillips Thygeson.

8

UVEA, SYMPATHETIC DISEASE, AQUEOUS

Kapuscinski, W. J., Jr. **Pyretotherapy as a diagnostic provocative in uveitis.** Arch. d'opht. **9**:27-30, 1949.

Kapuscinski uses typhoid vaccine intravenously in a technique devised by him which consists of a series of small doses increased gradually from .01 cc. to 1.0 cc. By this method he obtains a fever curve comparable to that of tertian malaria. He has found that in uveitis of tuberculous origin subjected to fever therapy there is usually an aggravation of the local eye lesion, an increase in the sedimentation rate, and sometimes a manifest oscillation of the daily tempera-

ture curve. In nontuberculous uveitis the fever therapy usually results in an acceleration of the sedimentation rate but does not change the daily temperature curve and affects the eye lesion favorably. In a series of 40 cases only four could be considered tuberculous. Fifteen cases are described in detail. The most frequent cause of uveitis is a streptococcal granuloma in a dead tooth or in the tonsils.

Phillips Thygeson.

Malbrán, J. L., and Rebay, C. A. **Rubeosis iridis and anterior glaucoma of Contino and Favaloro.** Arch. de oft. de Buenos Aires **23**:276-291, Oct., 1948.

Rubeosis iridis is characterically seen in many diabetics on the anterior surface of the iris, from the root to the pupillary zone, as many radially arranged thin vessels that do not invade the pigmentary pupillary epithelium nor quite reach the angle of the anterior chamber, which description coincides with Salus' original observations. The ocular tension is often elevated. This syndrome may be more completely described as follows: painful glaucoma, deep anterior chamber, iris turbidity with new-vessel formation as described above, dilated pupil, with or without anterior chamber hemorrhage, and venous hyperemia. The authors point out that rubeosis may or may not exist with or without glaucoma and that the glaucoma may appear in patients without diabetes as well as in diabetics. Thirteen cases are described in detail and the important findings are tabulated. (4 figures, 1 table, 25 references.)

Edward Saskin.

Tower, P. **Traumatic choroiditis.** Arch. Ophth. **41**:341-352, March, 1949.

Ten cases of so-called rupture of the choroid are reported. The etiology and pathology of these lesions are discussed. Discontinuity of the choroid following indirect injury to the eyeball is shown to be due to necrotic changes of trophic character. A more precise terminology is proposed; "arciform traumatic choroiditis" is suggested for crescentic lesions and "diffuse traumatic choroiditis" for those of irregular outline.

Ralph W. Danielson.

9

GLAUCOMA AND OCULAR TENSION

Bloomfield, Sylvan. **The lability test: a new procedure for the diagnosis of chronic simple glaucoma.** New York State J. Med. **49**:659-662, March 15, 1949.

The test combines the cold presser test of Hines and Brown and the jugular compression test described by Schoenberg. The patient lies flat on the table and one hand is immersed to the wrist in ice water. A blood pressure cuff around the neck is inflated to a pressure of 50 to 60 mm. Hg so that both jugular veins are compressed simultaneously. After one minute the tension is recorded. A rise of more than 9 mm. Hg (Schiøtz) above the ocular tension taken just before the patient immerses his hand in the ice water is a reliable aid in making a diagnosis of chronic simple glaucoma in that eye. This test compares very favorably with the other provocative tests now in use. The responses are greater and more easily recognized than those from the other tests in use. (4 figures.)

H. Weinberg.

Bonavolontà, Aldo. **Ophthalmoscopic examination with red-free light in glaucoma.** Ann. di ottal. e clin. ocul. **74**:459-478, Aug., 1948.

In prodromal and incipient glaucoma slight fading of the macular yellow and diminution of the foveal reflex may be noticed, but nothing is found that might not be expected in the eyes of any elderly person. In more advanced cases the nerve fibers become attenuated and undergo fragmentation, and ultimately the pattern

of the nerve fiber layer is lost altogether and replaced by a marbled appearance, and likewise the foveal reflex becomes irregular in form, luminosity, and direction of movement, and may completely disappear. The macular yellow is also reduced or absent. Chronic simple and congestive glaucoma cannot be differentiated from each other by this means, but in the latter type the macula and the papillomacular bundle tend to be involved earlier and more extensively, whereas in chronic simple glaucoma the temporally situated nerve bundles may show the greater damage. The changes noted in glaucoma cannot be sharply distinguished from those found in atrophy of the optic nerve or macular degeneration due to other causes. (3 colored plates.)

Harry K. Messenger.

Raimondo, N. **Fuchs's heterochromia with glaucoma: pathogenetic considerations.** Ann di ottal. e clin. ocul. **74**:423-435, July, 1948.

Raimondo reports two cases of Fuchs's heterochromia with glaucoma. The association of these two diseases is very rare. In one of his cases a bit of iris excised in trephining showed dystrophy of the stroma and rarefaction of pigment in the anterior limiting layer, conservation of the retinal pigment, thickening of the walls of the small vessels and capillaries, but no inflammatory changes. Raimondo's opinion is that both diseases are to be ascribed to congenital asymmetry in sympathetic innervation, which favors a vasomotor disequilibrium. (References.)

Harry K. Messenger.

10

CRYSTALLINE LENS

Barkan, Otto. **Operation for congenital cataract.** California Med. **70**:274-277, April, 1949.

Refinements in linear cataract extraction are described in detail. The pupil is maximally dilated preoperatively with atropine and subconjunctival adrenalin. A flat corneal incision is made with a keratome, the lens is removed extracapsularly and saline solution or air is used to refill the anterior chamber.

Orwyn H. Ellis.

Meyer, F. **The origin of the X-ray cataract.** Klin. Monatsbl. f. Augenh. **114**: 33-36, 1949.

The author describes the development of cataract as a result of repeated exposure to small doses during the calibration of instruments. Summation of small amounts of X ray produced the lesion.

Max Hirschfelder.

Redl, T. **A family with partly presenile, partly infantile hereditary cataract.** Klin. Monatsbl. f. Augenh. **114**:24-33, 1949.

The author reports the appearance of cataract in a family which he traced through seven generations. Intermarriage occurred on at least four occasions. Presenile cataract appeared in one member of the second generation and occurred in the third and fourth generation. Several members of the fifth, sixth and seventh generation sucered from congenital perinuclear (lamellar) cataract. The change in the type of cataract occurred in one generation, the fifth. The mode of inheritance is the "mixed form" of Groenouw. (Reference, 1 family tree.)

Max Hirschfelder.

11

RETINA AND VITREOUS

Cremona, A. C., and Manzitti, E. **Biogenic treatment of pigmentary retinosis.** Arch. de oft. de Buenos Aires **23**:309-312, Oct., 1948.

When parts of the body are isolated from their usual vascular and nervous connections they are said to develop "biogenic stimulants." Pieces of tissue of the

cornea, choroid, retina, cerebrum or placenta may be removed from the newly-dead and refrigerated. These may then be implanted beneath the skin or conjunctiva, or may be administered as an intramuscular injection. Intramuscular injections of placental extract were given to 33 patients with pigmentary retinosis with improvement in 13. (2 tables.)

Edward Saskin.

Eross, S., and Tarjan, G. **Retinal blood pressure in gravidic intoxications.** Orvosi Hetilap **26**:406, Sept. 26, 1948.

In 41 gravid women with disturbances of the kidney or cardiovascular system, discordant values between the diastolic pressure of the central retinal artery and the brachial were found. Among these, 13 had eclampsia, in 3 intrauterine death of the fetus occurred, and one had myodegeneration of the heart, and lues. Concordant values were found in two pregnant women with essential hypertonia. In 50 healthy pregnant women they found no discordant values. The proportional rise of diastolic blood pressure in a retinal artery in severe nephropathia is a warning sign. In patients who had proportional diastolic pressure in the retinal artery the nephropathy did not become worse during pregnancy or delivery. (2 figures.)

Gyula Lugossy.

Fleischer, Eberhard. **Four new cases of Aguchi's disease.** Klin. Monatsbl. f. Augenh. **110**:296-302, May-June, 1944.

All patients were males between 9 and 25 years old. There was pronounced night blindness since early childhood. Vision, visual fields and color sense were always normal. There were areas of grayish discoloration in the fundus, especially in the periphery. Mizuo's color-change was positive. After one hour in the dark the fundus looked normal, but changed to the original appearance after exposure to daylight. The dark adaptation was very much delayed, but after three hours or more the values were normal. The change of the gray to normal fundus and the dark adaptation do not take place at the same rate but the cause of both is probably an abnormal breakdown and regeneration of the visual purple. The transmission is recessive and not sex-linked.

George Brown.

Friedenwald, J. S. **A new approach to some problems in retinal vascular disease.** Tr. Am. Acad. Ophth. pp. 73-87, Nov.-Dec., 1948.

A new staining method (Hotchkiss) which demonstrates fixed carbohydrate is applied to ocular tissues. Any cellular structure containing carbohydrate stains red. Structures taking the stain include conjunctival goblet cells, Bruch's and Descemet's membranes, lens capsule, the subepithelial basement membrane of the ciliary processes, the internal limiting membrane of the retina, and, to a lesser extent, the peripheral portion of the rods and cones. The entire retinal vascular tree has a subendothelial membrane which is readily demonstrable. It is broadest in the arterioles, and less in the venules, and thinnest in the capillaries. Its breadth and stability vary with the age of the individual rather than that of the vessel. Two capillary systems are demonstrable in the peripapillary zone of the retina. One is in the nerve fiber layer and has a rectangular configuration; the other is an irregular network in the inner nuclear layer. Only the latter persists peripherally. Capillary aneurysmal dilatations occur most frequently at the posterior pole and in the inner nuclear layer. They are consistently found in diabetic retinopathy and only rarely in other retinopathies. The development of the aneurysms is briefly discussed, and an analysis drawn between the endothelial changes of Kimmelstiel-Wilson intercapillary glomerulosclerosis.

A histochemical investigation of the cotton-wool patches frequently seen in malignant hypertension is briefly discussed. They occur at the posterior pole and in the nerve fiber layer. These lesions were shown to be globular cytoid structures and to represent minute ischemic infarcts in terminal arteriolar bifurcations. Resorption is the usual course. The Hotchkiss staining procedure and its adaptation to ophthalmic uses is described in detail. Preparation of the reagents employed is outlined.

Chas. A. Bahn.

Grossmann, E. E., and Hitz, J. B. **Lipemia retinalis associated with essential hyperlipemia.** Arch. Ophth. **40**: 570-573, Nov., 1948.

Since its first description, in 1880, about 60 cases of lipemia retinalis have been reported in the literature, and it is noteworthy that all have been in diabetic patients. The rare nondiabetic lipemia retinalis is associated with idiopathic hyperlipemia and is probably a familial anomaly of lipid metabolism that occurs in children. This case is the fifth recorded instance of lipemia retinalis in a nondiabetic person, and is probably the first in a nondiabetic adult.

Ralph W. Danielson.

Guyton, J. S., and Reese, A. B. **Use of roentgen therapy for retinal diseases characterized by new-formed blood vessels (Eales' disease; retinitis proliferans): a preliminary report.** Arch. Ophth. **40**: 389-412, Oct., 1948.

Intensive roentgen therapy to the posterior ocular segment was given in a series of patients with ocular diseases characterized by retinal and vitreous hemorrhages and by retinitis proliferans. Twenty-two eyes in 14 patients were treated. There was typical Eales' disease in 8 patients, atypical in 4, and diabetic retinitis proliferans in 2. The method devised by Martin and Reese for the treatment of retinoblastoma was used to avoid damage to the anterior ocular segment. A dose of 3,500 to 15,000 r was given each eye treated; doses of 6,000 r are probably optimal. There was moderate to complete collapse of new-formed vessels and variable regression of fibrosis. There has been only one recurrent hemorrhage since the treatment in the 8 cases of typical Eales' disease. In the patients with diabetic retinitis proliferans, hemorrhages have continued to appear.

John C. Long.

Van Heuven, J. A. **Detachment of the retina following inflammation.** Tr. Ophth. Soc. U. Kingdom. **66**:493-500, 1946.

A detachment of the retina about three months after an acute iritis showed a vitreous strand along the course of a vessel. No hole in the retina was visible for several days. Later a hole appeared and was cauterized. Beulah Cushman.

Hollenhorst, R. W., and Wagener, H. P. **The effect of rutin in the control of bleeding into the retina.** Am. J. M. Sc. **217**:223-231, Feb., 1949.

The authors give a résumé of the work done on the treatment of retinal hemorrhages, especially those associated with increased fragility of the minute vessels of the skin, by such substances as citrin, hesperidin, and rutin. Rutin may decrease capillary fragility but it is not certain that increased fragility and permeability of the skin capillaries are accompanied by corresponding dysfunction of the retinal capillaries, especially in diabetic retinopathy. Some retinal hemorrhages may arise from a vitamin P deficiency. Evaluation of clinical improvement in the retina is most difficult. Superficial hemorrhages may be absorbed spontaneously in a short time, deeper ones may persist for a year or more, and all types frequently recur.

Rutin therapy in retinal complications of diabetes has been discouraging due to the deep location and the slow progress of the disease. In many other diseases the hemorrhages are more superficial and hence absorbed more rapidly. The value of rutin in retinal disease of diabetics is very doubtful. F. M. Crage.

Kinsey, V. E., and Zacharias, L. **Retrolental fibroplasia.** J.A.M.A. **139:** 572-578, Feb. 26, 1949.

Since this disease was first associated with prematurity by Terry in 1942, there has been an increase in the number of cases reported which cannot be fully explained by the statement that the condition was formerly undiagnosed or missed, or that more premature infants survive now than before. Various factors were investigated which might have influenced this increase. The incidence of disease was higher in children born of multiparous women and in infants who remained in the nursery, incubator, and oxygen for longer than usual and also higher in the male. It might be of etiologic significance that the incidence was greatest during a time when there was increased use of vitamin in water-miscible form, and of iron. (14 tables.)

Bennett W. Muir.

Kreibig, W. **Clinical demonstration of calcium deposits in retinoblastoma.** Klin. Monatsbl. f. Augenh. **114**:84-89, 1949.

Early necrosis of the gliomatous tissue often leads to calcium deposits in the intraocular part of the tumor. The author found these deposits in 16 of 20 eyes by histologic examination. No other intraocular tumor shows calcification, a fact which is of differential diagnostic significance. These calcium deposits form very soft shadows on the X-ray film. Positive findings remove all doubt. (7 figures, references.)

Max Hirschfelder.

Levitt, J. M. **Occlusion of the cilioretinal artery.** Arch. Ophth. **40**:152-156, Aug., 1948.

Occlusion of the cilioretinal artery in a 19 year old woman is described. There was loss of central vision, a broad band of retinal edema between the optic nerve and macula and a large cecocentral scotoma. Intensive use of vasodilators was followed by almost complete recovery. John C. Long.

Lijó Pavía, J. **Solar retinitis. Macular study with sodium light.** Rev. oto-neuro-oftal. **23**:71-78, Oct.-Dec., 1948.

In a previous paper the author established the fact that phototrauma of the eye results in a hole of the macula and central scotoma. Four cases of exposure to solar eclipse are presented now, each carefully studied with ordinary, red-free, and sodium light. The latter type of examination corroborated the findings with ordinary and red-free light, namely, mild optic neuritis, general retinal edema, alteration of the papillomacular fibers, marked central retinal edema, and a hole in the fovea. However, the pathologic picture was most readily appreciated in stereoretinography in yellow light. In all four cases visual acuity returned to normal in 20 to 68 days. (2 stereoretinographs.) Edward Saskin.

Lijó Pavía, J., and Cabrera, M. **Vitreous humor substitution.** Rev. oto-neuro-oftal. **24**:13-17, Jan.-Feb., 1949.

The authors' surgical procedure is performed under pentothal and consists of an equatorial scleral incision through which 1.50 cc. of vitreous is removed by syringe and an 18 gauge needle. The syringe is then removed but the needle is left in situ, and 2 cc. of clear donor vitreous from an enucleated eye in another syringe is injected into the vitreous cavity through the same needle. The

scleral incision is then sutured. In an only eye with turbid vitreous visual acuity improved from perception of shadows to 20/200. Edward Saskin.

Linde, L. **Prophylactic surgery for potential retinal detachment.** Klin. Monatsbl. f. Augenh. **113**:140-142, 1948.

The case histories of five patients in whom a prophylactic fixation of the retina was necessary are presented. The author recommends such surgery in all cases of retinal tears, whether detachment has occurred or not. It is imperative to investigate such an eye carefully for new tears even after seemingly successful surgery and the other eye as well. Prophylactic diathermy surgery also has a place in eyes that are inclined to retinal detachment. In a patient with Marfan's syndrome such prophylactic fixation was done and no detachment followed surgery for a dislocated lens. This type of surgery is harmless and obviates perforating procedures. Max Hirschfelder.

Loewenstein, A., Michaelson, J. C., and Hill, J. **Retinal vasculitis of the young: a pathological report.** Tr. Ophth. Soc. U. Kingdom **66**:211-230, 1946.

The author reports the pathologic findings in two eyes with retinal vasculitis. The eyes had been enucleated in young people because of glaucoma. Histologic studies revealed numerous retinal hemorrhages, ectasia of the retinal vessels and venous stasis. Hemorrhages were present in the thickened vessel walls. There was extensive granulomatous infiltration of many venous walls. The choroid was normal. Numerous sections were stained with Ziehl-Neelsen's stain but no acid fast bacilli were found. Animal experiments suggest the presence of an infective agent in the retina. It is suggested that the use of retinal tissue for biological experiment may be a fruitful approach to the problem of causation. (19 figures.)
Beulah Cushman.

Maggiore, L. **Histologic changes in retinal edema.** Ann. d'ocul. **181**:681-691, Nov., 1949.

The most important factors in injury to the retina caused by edema are the intensity and duration of the edematous infiltration, its location, the coexistence of hemorrhage, and the coexistence of toxic or infectious disease. Variations in the degree of edema determine the degree of structural damage to the retina and whether vision is temporarily or permanently injured. Edematous infiltration of the fibers of Henle's layer may cause a hole in the fovea, an important factor in some cases of retinal detachment. The disposition of the fibers of Henle's layer in the macular region explains how intense edema can pull apart these fibers without causing rupture at the periphery of the fovea, whereas at the center, where the fibers are short and lie perpendicularly, stretching will tear them and produce a hole. If the edema is limited to the internal layers of the retina the hole will be superficial and the detachment intraretinal; if a massive edema infiltrates even the visual cells, the hole will penetrate the foveal retina throughout its thickness and will be complete, that is, a true retinal detachment.
Chas. A. Bahn.

Malatesta, C. **Two cases of pigmentation of the disc after retinal detachment operation.** Boll. d'ocul. **32**:722-733, Nov., 1948.

Two men, aged 49 and 57 years, had extensive dispersed pigmentation of the retina and the optic discs after diathermy coagulation for retinal detachment. The pigmentation appeared a few days after the operation and disappeared gradually in a month. (2 colored drawings.)
K. W. Ascher.

Malbran, and Montalvan. **Pseudoforamina of the macula in disinsertions of the ora serrata.** Arch. de oft. de Buenos Aires **23**:252-258, Sept., 1948.

There is little in the literature on the association of dialysis of the ora serrata with a pseudoforamen of the macula which was first described by Vogt in 1936, and is of interest in diagnosis, prognosis and therapy. Six cases are reported.

This is one of the forms of cystic degeneration of the macula. There is a reddish discoloration at the macula of variable size. The edges are clear-cut and surrounded by pale and edematous retina. The macular region is raised as if by a single or multiple tense vesicle of variable transparency. There is a foveal reflex because the internal limiting membrane is preserved. Fine striations extend outward from the macula. Differentiation from a traumatic or spontaneous hole at the macula is at times difficult. A. G. Wilde.

Marín Amat, M. **Spasm of a cilio-retinal vessel, and of the superior branch of the central retinal artery.** Arch. Soc. oftal. hispano-am. **9**:91-93, Jan., 1949.

A woman had an ophthalmoscopically visible spasm of a cilioretinal artery with a total loss of the lower half of the visual field. After treatment with vasodilators vision was restored, and only slight pallor of the disc, and a slight constriction of the upper retinal vessels remained. Treatment must not be abandoned too early, persistence frequently leads to surprizing results. (3 visual fields.) Ray K. Daily.

Mariotti, Lorenzo. **Intravenous procaine and para-aminobenzoic acid in the treatment of thrombosis of the central retinal vein.** Ann. di ottal. e clin. ocul. **74**:350-357, May, 1948.

Mariotti reports three cases of thrombosis of the main branch of the central retinal vein, and nine of thrombosis of a branch of the vein, in which 20 to 180 mg. of procaine were given in 2 to 18 intravenous injections of a 1- or 2-percent solution at intervals of a day or more. This therapy was ineffective in thrombosis of the trunk, but in the other cases the results were encouraging. The systemic systolic pressure, the retinal arterial pressure, and the ocular tension were always reduced. The efficacy of procaine in dislodging the thrombus seems to be due in great part to its vasodilator action. Presentation of the results obtained with para-aminobenzoic acid is reserved for another paper. Harry K. Messenger.

Moreu, Angel. **Observations on the pathogenesis and treatment of diabetic retinopathy.** Arch. Soc. oftal. hispano-am. **9**:139-146, Feb., 1949.

The physiologic action of hyalouronic acid and hyalouronidase is reviewed. The development of diabetic retinopathy is attributed to variations in the sugar metabolism, caused by injudicious use of insulin. Hypoglycemia stimulates the production of hyalouronidase which destroys hyalouronic acid, and increased fragility of the vessel walls and hemorrhages follow. In the hyperglycemic phase an excess of hyalouronic acid stimulates the organization and proliferation of connective tissue. It is urged that insulin be used with great caution and that more attention be paid to capillary fragility. Agents that improve cellular respiration such as heparin are indicated.

Ray K. Daily.

Oravisto, T. **The ocular symptoms of arterial hypertension.** Ophthalmologica **117**:161-168, March, 1949.

The author reports his examination of 70 patients under 50 years of age with pure essential hypertension and as little sclerosis as possible. The classification of hypertensive cardiovascular disease according to Keith-Wagener is recom-

mended as a basis for cooperation between the internist and ophthalmologist.

Peter C. Kronfeld.

Reese, A., and Blodi, F. **Retrolental fibroplasia.** Klin. Monatsbl. f. Augenh. **114**:18-24, 1949.

Three groups of retrolental fibroplasia are discussed. Dysplasia of the retina is a bilateral malformation with persistence of the primary vitreous and lack of formation of the secondary vitreous. It is often associated with other malformations of the brain and the vascular system. Hyperplastic primary vitreous is usually unilateral and characterized by hyperplasia in the central retrolental region. True retrolental fibroplasia forms a third group which has increased in frequency during the past few years. Persistence of the primary vitreous leads to a dense grayish tissue formation behind the lens with its densest parts near the equator of the lens. The lens itself stays clear. Detachment of the retina is found in the final stages. The disease is always bilateral and prevalent among premature children. The theories of its etiology and the therapy are discussed. (References.)

Max Hirschfelder.

Schiff-Werthheimer, S., Jonquères, J., and Jarry, C. **Retinal detachment of young myopes.** Ann. d'ocul. **182**:13-23, Jan., 1949.

The prognosis and symptomatology of 49 patients under 30 years of age with an average myopia of 12D are described. The prognosis is worse in the younger group. After operation, one third had a corrected vision of 0.1 or more and almost one half had no vision. Multiple tears are more frequent than in unselected cases and bilateral detachment is more frequent in the young. Chas. A. Bahn.

Tirelli, G. **A case of macular hole following rapid lowering of atmospheric pressure.** Rassegna ital. d'ottal. **17**:353-356, Nov.-Dec., 1948.

A 30-year-old man, a former aviator and Alpinist, suffered an epistaxis, rapidly followed by a sudden loss of vision while mountain climbing at an altitude of 4,000 meters and after passing through a severe storm. The ophthalmoscope disclosed a round hemorrhage at the macula of the left eye. In all other respects the eyes were healthy. Two months later, the hemorrhage was absorbed leaving a clear-cut, round hole, one half the disc diameter in size, exactly at the macula. The author assumes that the diminished atmospheric pressure and the low barometric pressure accompanying the storm and increased capillary fragility from severe fatigue caused the hemorrhage.

Eugene M. Blake.

Unsworth, A. C. **Retrolental fibroplasia.** Arch. Ophth. **40**:341-346, Sept., 1948.

In observing the eyes of premature infants from birth, the author rarely saw remnants of the hyaloid artery but they appeared shortly. Of 30 premature infants none was born with a retrolental membrane. In two infants that he saw shortly after birth without evidence of ocular abnormality, retrolental fibroplasia has since developed. He believes that retrolental fibroplasia as it is usually known is not congenital. In one case, at least, the mechanism of its formation was seen to be leakage of blood from the retinal vessels into the vitreous, followed by vascularization of the hemorrhage in the vitreous from the retinal vessels. Remnants of the hyaloid artery were not persistent in any of these cases and certainly played no part in the formation of the angioplasia of the vitreous. He feels sure that this condition, if untreated, will become a typical retrolental fibroplasia by spreading over the posterior surface of the lens. This formation seems to be akin

to the formation of granulation tissue elsewhere in the body, to retinitis proliferans or to the syndrome of von Hippel's angiomatosis. The anemia of prematurity in itself may be a factor in the causation of retrolental fibroplasia. There seem to be two main types. The first develops from the proliferation of vascular tissue from the retinal vessels of the posterior portion of the fundus into abnormal vitreous. The second is the result of failure of development or condensation of the secondary vitreous at the anterior periphery, with proliferation into it of retinal vessels from the unattached peripheral portion of the retina.

Ralph W. Danielson.

Verhoeff, F. H. **Successful diathermy treatment of recurring retinal hemorrhage and retinitis proliferans.** Arch. Ophth. **40**: 239-244, Sept., 1948.

Recurring retinal hemorrhage in the young is frequently associated with ophthalmoscopically recognizable periphlebitis. Usually there is a cutaneous reaction to tuberculin, and nodular foci of epithelioid cells along the veins have been observed. Histologically there is strong evidence that tuberculosis is the cause. The hemorrhage evidently results from engorgement of capillaries and small veins and when it is severe and persistent, new vessels are formed, which may extend into the vitreous. Hemorrhage into the vitreous usually occurs, and the blood becomes organized, thus producing typical retinitis proliferans. The author reports in detail the successful use of diathermy in such a case.

Ralph W. Danielson.

Wagner, E. **A late form of familial amaurotic idiocy in a brother and sister.** Klin. Monatsbl. f. Augenh. **114**:37-42, 1949.

There was no sign of retinitis pigmentosa. The brother showed a secondary optic atrophy, concentric contraction of the field and colorblindness. Neurologic investigation by means of X ray, encephalograms and biopsy revealed increased intracranial pressure and the damage to the ganglion cells of the cortex characteristic of familial amaurotic idiocy. The sister who had a normal mind had a nystagmus, was colorblind and had a pituitary form of adiposity.

Max Hirschfelder.

13

NEURO-OPHTHALMOLOGY

Becker, F. Y. **Herpes zoster ophthalmicus: results of treatment with transfusions of convalescent blood.** Arch. Derm. and Syph. **58**:265-275, Sept., 1948.

The author reports six cases of herpes zoster ophthalmicus treated successfully by the method of Gunderson, who gives 250 to 450 cc. of convalescent blood intravenously early in the disease, preferably before involvement of the eye. Herpes zoster is probably caused by a virus because recurrences are unusual, inclusion bodies are present in the vesicles, and there are antibodies in the serum of convalescent patients. However, because the agglutinins do not appear until the third week, convalescent serum should be given early. After transfusion, the temperature becomes normal, pain is alleviated, the edema and infiltration are decreased, the patient is less toxic, and the ophthalmic lesions begin to heal.

R. Grunfeld.

Bridges, T. J., Pool, J. L., and Riley, C. M. **Central autonomic dysfunction with defective lacrimation. II. Preliminary report of effect of neurosurgery in one case.** Pediatrics **3**:479-481, April, 1949.

A division of the tentorium on the right side was performed on a 4-year-old boy

with defective lacrimation and central autonomic dysfunction. Lacrimation made its appearance on the sixth postoperative day and has persisted. The lability of blood pressure and the abnormal reactions disappeared immediately, only to return after a period of three weeks.

I. E. Gaynon.

Fonte Barcena, A., and Manzilli, E. **Ophthalmoplegic migraine.** Arch. de oft. de Buenos Aires **23**:233-239, Sept., 1948.

Typical ophthalmoplegic migraine that occurred in a 51-year-old woman is described and our meager knowledge of the syndrome is discussed. A. G. Wilde.

Freymann, M. W., and Bang, F. B. **Human conjunctivitis due to Newcastle virus in the U.S.A.** Bull. Johns Hopkins Hosp. **84**:409-413, May, 1949.

Three laboratory workers developed conjunctivitis with preauricular adenitis due to the virus of Newcastle disease in chickens. Virus was isolated in two of the eyes. The course was brief, without complication, and lasted three to five days. I. E. Gaynon.

Guthkelch, A. N. **Extradural hemorrhage as a cause of cortical blindness,** J. Neurosurg. **6**:180-182, March, 1949.

A case of almost total cortical blindness due to bilateral occipital extradural hematoma is recorded.

Miss L. K., 67 years old, struck the back of her head. She was drowsy and irritable. Xrays revealed a fissured fracture. After four days her conscious level improved, but she complained of blindness. Ten days later she was garrulous, euphoric and devoid of insight. The discs showed acute papilledema with hemorrhages, but no exudate and the pupils were normal. A diagnosis of bilateral occipital subdural hematoma was made. At operation a huge black clot was removed from the extradural space. Two days later the visual acuity improved and on the fourth day she could read a newspaper comfortably. When last seen one year later her health was excellent and she was able to do fine work as well as ever. Her visual fields remained full and the optic discs had returned to normal.

Theodore M. Shapira.

Jensen, Jens. **A case of herpes zoster ophthalmicus complicated with neuroretinitis.** Acta opth. **26**:551-558, 1948.

Herpes zoster ophthalmicus occurred in a 9-year-old girl after she was exposed to varicella during an epidemic. The disease was complicated by optic neuritis, retinitis, internal ophthalmoplegia, optic atrophy and macular changes. The literature on similar complications of herpes zoster is reviewed. Ray K. Daily.

Lijó Pavía, J. **Photographic documentation of nystagmus.** Rev. oto-neuro-oftal. **24**:9-11, Jan.-Feb., 1949.

Three photographically documented cases of nystagmus are presented. A speed of 64 frames per second leaves much to be desired; 200 per second will yield a more revealing slow-motion analysis of the details of nystagmus.

Edward Saskin.

Paufique, Mayoux, Hugonnier, and Aubert. **Parinaud's syndrome associated with vertigo.** Ann. d'ocul. **182**:1-12, Jan., 1949.

A man, aged 49 years, noted transient diplopia for about three hours. Subsequently he developed a bilateral paralysis of elevation and convergence with vertigo. Parinaud's syndrome is apparently due to a lesion in the posterior white commissure of the pons. The vertigo was believed due to a lesion in the vestibular nucleus, probably near the nuclei of Bechterew and Deiter. The cause was

probably a vascular disturbance. The blood supply of the pons includes rubopyramidal, oculo-nuclear and lateral sulcus arteries. Chas. A. Bahn.

Riley, C. M., Day, R. L., Greeley, D. M., and Langford, W. S. **Central autonomic dysfunction with defective lacrimation. I. Report of five cases.** Pediatrics **3**:468-478, April, 1949.

A syndrome consisting of diminished to absent lacrimation, hypertension, skin blotching, drooling, cold hands, cyclic vomiting, mental retardation and hyporeflexia in children is presented. The findings seem best interpreted as a central, possibly congenital, disturbance of autonomic function. (1 table.)

I. E. Gaynon.

Sitler, R., Cremona, A., and Manzitti, E. **Myasthenia of visual type.** Arch. de oft. de Buenos Aires **23**:226-232, Sept., 1948.

A four-year-old boy had equal and progressive bilateral ptosis, since he was two and a half years old. He was able to open the eyes during the early morning hours, but this power decreased during the day. There was also an almost complete immobility of the eyes. The excursion of the gaze was about two millimeters. No other symptoms were demonstrable. The distinguishing feature of this disorder is a rapidly increasing fatigability of the involved muscles, which improves after variable periods of rest. It is necessary to differentiate myasthenia from congenital ophthalmoplegia and the chronic external type, which is progressive. A diagnostic aid is the dramatic improvement or even temporary disappearance of symptoms after prostigmin. A. G. Wilde.

Spadavecchia, Vitangelo. **Nasociliary neuritis.** Ann. di ottal. e clin. ocul. **74**: 321-338, May, 1948, 436-455, July, 1948.

The first installment of this monograph was abstrated in Am. J. Ophth., Sept., 1942.

Four types of nasociliary neuritis are recognized: the simple irritative, the irritative-inflammatory, the atrophic, and the postinflammatory atrophic-degenerative. Our knowledge of the pathogenesis of this disease is much limited by the absence of histopathologic material and by our ignorance of the reciprocal influence between the central and the autonomic nerve fibers in the nasociliary region. Neuritic pain, photophobia and blepharospasm are referable to cerebrospinal elements, whereas vasomotor and secretory disturbances point to autonomic involvement. The symptoms are so typical that the diagnosis is easy, but in making a differential diagnosis it is necessary to eliminate neurosis, simple nasociliary irritation, lesions of the fifth cranial nerve, certain types of headache, and acute glaucoma. Symptomatic treatment of pain is indicated, and cocainization and adrenalization of the nasal fossa are of value. Intranasal foci or spurs causing irritation should be treated surgically, and in severe cases the injection of alcohol in the region of the nasociliary nerve is advised. (References.)

Harry K. Messenger.

14

EYEBALL, ORBIT, SINUSES

Belmonte-González, Manuel. **Hydatid cyst of the orbit.** Arch. Soc. oftal. hispanoam. **9**:49-59, Jan., 1949.

A diagnosis of a hydatid cyst of the orbit was made in a woman 24 years old, with a rapid onset of exophthalmos, diplopia, displacement of the eyeball downwards, choked disc, and loss of vision and the absence of rhinologic and roentgenologic signs of paranasal sinusitis. The cyst was exposed through a canthotomy, punctured, evacuated and filled for a few minutes with a 1-percent solution

of formalin (its deep location precluded complete extirpation) and the wound was sutured and drained. The patient recovered with recession of the choked disc, restoration of vision but with restriction of lateral rotation, and diplopia. (3 figures.) Ray K. Daily.

Buesa, Lorente. **A case of thrombophlebitis of the cavernous sinus.** Arch. Soc. oftal. hispano-am. **9**:34-48, Jan., 1949.

An acute fulminating case of thrombosis of the right cavernous sinus is reported in a man, 46 years old. The infection originated in the last right lower molar tooth and advanced through the inferior dental veins. It was complicated by an orbital abscess which drained spontaneously at the inner canthus. In addition to the classical symptoms there was myosis of the right eye which is attributed to a venous stasis in the iris and a paresis of the sympathetic fibers in the first branch of the trigeminal. The patient recovered under treatment with penicillin and sulfa drugs. Ray K. Daily.

Hughes, W. L. **Metallic implants and integrated artificial eyes.** Plast. and Reconstruct. Surg. **4**:175-177, March, 1949.

The author has originated four types of Vitallium implants for use with integrated artificial eyes. They have a flat face with depression anteriorly to receive the peg on the posterior surface of the eye. No reaction has been noted from these implants. Few extrusions have occurred, and in them the usual buried implant was used. Alston Callahan.

Larsson, H., Lindblom, K., and Stenström, S. **Clinical and roentgenological view regarding the localization of foreign bodies in the orbit.** Acta ophth. **26**:557-580, 1948.

This symposium consists of 3 papers. Stenström discusses the relation of variations in the size and shape of the eye to the accuracy of roentgenographic localization. He reports graphically the data of measurements of the vertical diameter of the eyeball in 1,000 cases, and of the horizontal diameter in 766. The vertical diameter was determined by Rushton's method, and the horizontal measured with Berg's appliance. The charted data show that the size and form of the eyeball are subject to such marked variations that in cases requiring precise localization the determination of the length and equatorial diameter of the eyeball is indispensable.

Lindblom describes his method of bitangential roentgenographic localization without determination of the size of the eyeball. It consists in getting a shadow of the cornea on the film by surrounding it with air; the upper lid is elevated with a spring, and the lower lid fastened down with adhesive tape. The degree of magnification of the cornea in the radiographs is calculated from the focal film and focal eye distances. Outlines of normal eyeballs corresponding to the degree of magnification engraved on transparent film are placed on the radiograph and the distance of the foreign body from the coronal, sagittal, and horizontal midplanes of the eyeball measured. The relation of the foreign body to the cornea and sclera can be seen on the film.

Larsson's method of localization includes concurrent determination of the size of the eyeball. Various methods for determining the size of the eyeball are discussed, and preference expressed for a modification of Rushton's method. The modification consists in moving the eyeball forward to the X-ray beam, instead of moving the beam to the posterior pole of the eye. The shadow of the cornea is visualized on the same film which indicates the posterior pole of the eye with a dark streak; the axial length of the eye-

ball can thus be measured on the film. The apparatus and technique are described in detail. (12 figures.) Ray K. Daily.

Lisch, K. **Familial occurrence of spontaneous pulsating exophthalmous.** Ophthalmologica **177**:180-185, March, 1949.

Spontaneous (nontraumatic) pulsating exophthalmos was observed in a man, 23 years of age, and his sister, 45. In the latter the disease occurred bilaterally. The father of the two patients developed sudden unilateral proptosis at the age of 47 and died of apoplexy two years later. A hereditary predisposition to arterial rupture is assumed.

Peter C. Kronfeld.

Pallarés, J. **A case of sarcoma of the orbit, with diagnostic puncture and microscopic study of the fluid.** Arch. Soc. oftal. hispano-am. **9**:60-67, Jan., 1949.

The diagnosis of intraorbital sarcoma in an infant, 29 months old, was made from a cytologic study of material aspirated through a puncture of the tumor. After aspirating the fluid with a syringe, a diathermy current was passed through the needle for 15 seconds.

Ray K. Daily.

Pallestrini, Ernesto. **Blepharospasm and palpebral tic from sinusitis.** Riv. otoneuro-oftal., **23**:275-283, July-Aug., 1948.

A woman, 35 years of age, had unilateral fronto-maxillary sinusitis with homolateral blepharospasm. The spasm disappeared after the sinuses were clear. Three years later with recurrence of sinusitis there was bilateral blepharospasm together with spasm of the frontalis muscle and lacrimination under strong light. After radical surgical operation on the sinuses, the spasmodic condition disappeared permanently. The mucous membrane of the sinuses was found to be thickened with pseudomixomatous degeneration. Melchiore Lombardo.

Waugh, D. B. **Ocular prosthesis, with special reference to the conjunctival sac.** M. J. Australia **1**:311-313, March 5, 1949.

It is important that the conjunctival slack present in both fornices be preserved following enucleation in order to preserve the palpebral fold and the facial characteristics of the person involved. An acrylic splint made from the impression of the closed eye which is to be excised should be slipped under the lid following surgery in order to prevent the upper lid from being drawn inward.

I. E. Gaynon.

15

EYELIDS, LACRIMAL APPARATUS

Bassenge, W. **Irrigation of the tearsac with penicillin in dacryocystitis.** Klin. Monatsbl. f. Augenh. **113**:363-366, 1948.

After a series of irrigations with penicillin solution (50 Oxford units per cc.) in 20 patients, an improvement in the bacterial flora of the sac was the rule and in some cases the bacterial findings became negative. Whenever there was a patent sack originally or after probing, penicillin seemed effective. Patients with closed tearducts cannot be cured by this treatment. However, preparatory penicillin irrigation has a favorable influence on subsequent surgery. Dacryorhinocystostomy is recommended. (References.) Max Hirschfelder.

Berke, R. N. **Motais-Parinaud type of operation for ptosis.** Arch. Ophth. **41**:324-333, March, 1949.

Utilization of the superior rectus muscle to correct ptosis in 35 cases of congenital ptosis gave an excellent result in 4 cases, a good result in 14, a fair result in 8, and no improvement in 9. In 16 of 22 cases in which the Motais-Shoemaker-Kirby technic was used, and in 10 of 13 cases in which the Parinaud-Young-Dickey procedure was employed, im-

provement followed. Utilization of the superior rectus to correct ptosis induced weakness of that muscle in 26 of 35 cases. Lagophthalmos in sleep was present in most of the cases of corrected ptosis, but no evidence of corneal ulceration occurred. This type of procedure should be used only for ptosis with complete paralysis of the levator palpebrae and integrity of the superior rectus muscle function.

Ralph W. Danielson.

Chabat, H. **Operation for trachomatous trichiasis by the conjunctival route.** Arch. d'opht. **9**:48-51, 1949.

Chabat favors the conjunctival route for the correction of trichiasis because 1, it does not mutilate the tarsus, 2, it leaves no externally visible cicatrix, and 3, it requires no assistant, thanks to the use of a simple lid everter with two hooks for the attachment of sutures. A conjunctival incision is made 0.5 cm. from the free border of the lid, extending through the tarsus only, and dividing the tarsus into two portions. The marginal portion of the tarsus is dissected free from the overlying muscle and skin up to the bulbs of the cilia, while the remaining portion is also dissected free, well into the angles but not into the tendon of the levator. Four mattress sutures are then placed in such a way as to bring the cut border of the tarsus into the sulcus formed between the marginal tarsal leaf and the overlying skin, the sutures presenting at the lid margin. This everts the cilia, producing an ectropion which lasts for several weeks. The author comments on the relative freedom from recurrences.

Phillips Thygeson.

Ferraris de Gaspare, P. **Congenital fistulas of the lacrimal sac.** Boll. d'ocul. **27**:739-745, Nov., 1948.

Two patients with congenital fistulas of the lacrimal sac were observed. Histologic examination of one showed a fistula lined by epithelial cells similar to those of the lacrimal ducts. (References.)

K. W. Ascher.

Lagrot, Félix. **Dermo-epidermic free grafts of the lids.** Ann. d'ocul. **182**:32-51, Jan., 1949.

The indications for this type of graft include cicatricial retractions, entropion-lagophthalmus, primary gangrene, injuries of the lids, and lid conditions secondary to facial or orbital disease. The author prefers general anesthesia. After a horizontal lid incision with dissection, four sutures are placed into the upper and lower margins, and held with artery forceps. A compress of vaseline gauze is used to form a temporary mold to cover the lid wound. A graft is taken from the inner side of the upper arm and placed on the mold. The upper and lower lid sutures are used to close the wound. In 17 operations there was no failure. Chas. A. Bahn.

Marcks, K. M. **Repair of defects produced by excision of tumors in the eye region.** Plast. and Reconstruct. Surg. **4**: 178-187, March, 1949.

The complete removal of the tumor is preferred to the biopsy of a small amount of tissue. Primary repair should be instituted in all surgical excisions. Six varied cases are presented by means of brief histories, description of surgical procedure, and 26 photographs but no drawings. Secondary repair is performed after it is certain there will be no recurrence or extension of the initial lesion.

Alston Callahan.

Moulié, H. B., and Baron, H. G. **Dacryocystorhinostomy in the young.** Arch. de oft. de Buenos Aires **23**:298-301, Oct., 1948.

Sac extirpation should not be performed in the young because a life time of annoyance follows. Dacryocystorhinos-

tomy may be done in the young in chronic dacryocystitis or narrowing of the terminal portion of the nasolacrymal canal, and is almost always successful.

Edward Saskin.

Nordenson, J. W. **Jean-Louis Petit and the mechanism of lacrimal drainage.** Arch. d'opht. **9**:5-8, 1949.

Nordenson reviews the studies of the celebrated French surgeon, Jean-Louis Petit, which were made in 1734 and published under the title of "Memoire on Lacrimal Fistula." Petit attributed the flow of tears into the nose to a siphon action of the lacrimal passages, and to action of the lids in closing the conjunctival sac and pressing fluid into the canaliculi. These theories need reëxamination in view of the data obtained from dacryocystorhinostomy. Neither complete incision of the canaliculus nor removal of the lacrimal sac interferes with lacrimal drainage. Petit's lid closure theory would explain the tear flow in such cases. After a review of the literature and a consideration of his own observations, Nordenson concludes that Petit's siphonal theory can only be accepted in rare cases in which the transport of tears occurs in spite of paralysis of the facial nerve, but the theory of lid closure has been unjustifiably disputed. If it is correct, dacryocystorhinostomy is indicated when the canaliculi have been slit.

Phillips Thygeson.

Pereyra, C. C. A., and Riva, A. **Conjunctivitis and palpebral itching.** Arch. de oft. de Buenos Aires **23**:259-271, Oct., 1948.

Palpebral itching is a definite entity, and may exist alone as a result of mechanical, chemical, or medicinal irritation, chronic conjunctivitis, epiphora, refractive errors, allergy, or from neuro- or psychogenic factors. If the complaint be associated with a systemic condition such as arthritis, diabetes, or endocrine dyscrasia, the latter should be given treatment as the possible initiating agency in addition to the therapy for the relief of the itching. The authors sometimes use the antihistaminic drugs.

Edward Saskin.

Shuttleworth, F. N. **An advocacy of external dacryo-cystorhinostomy.** Brit. J. Ophth. **33**:183-187, March, 1949.

British ophthalmologists have not generally adopted the Toti operation and the author presents the results in 60 cases with a recommendation that the operation be more generally done.

Morris Kaplan.

16

TUMORS

Arjona, J. **Sturge-Weber syndrome with ocular melanosis.** Arch. Soc. oftal. hispano-am. **8**:1207-1218, Dec., 1948.

A boy, 13 years old, had epilepsy, numerous angiomas, buphthalmos in the left eye, chronic glaucoma in the right and blue scleras. The tension in both eyes was normal, although the anatomic changes indicated that it must have been high at some time. He had a small sella turcica, and calcification about the occipital lobes. Gradual improvement in the epileptic seizures is ascribed to a diminution in the meningeal angiomas. Involution of the angiomas of the choroid probably accounts for the normal tension. The blue scleras caused by melanosis are attributed to an abnormal activity of melanoblasts because of excessive choroidal vascularization. The literature on the pathogenesis of Sturge-Weber disease is reviewed, and it is suggested that melanosis of the eyeball may be a fourth symptom in the syndrome of angiomas, ocular and cerebral disturbances. (5 figures.)

Ray K. Daily.

Bloch, F. J. **Retinal tumor associated with neurofibromatosis (von Reckling-**

hausen's disease). Arch. Ophth. **40**:433-437, Oct., 1948.

A classification of the ocular complications of neurofibromatosis is given. The author reports a retinal tumor in a 60-year-old man with neurofibromas of the trunk and extremities. The tumor was ophthalmoscopically identical with tumors seen in tuberous sclerosis. In nine years of observation the fundus picture has not changed. John C. Long.

Costi, C. **Multiple teratoid dermoids.** Arch. Soc. oftal. hispano-am. **9**:28-33, Jan., 1949.

An unusual case of multiple teratoid dermoids in the lids and on both eyeballs of a child, 20 months old, is reported. The diagnosis was made by biopsy. (4 figures.) Ray K. Daily.

Moehle, W. **Myxosarcoma of the eyelid.** Arch. Ophth. **41**:317-323, March, 1949.

This myxosarcoma of the eyelid apparently resulted from trauma. There was no evidence of abnormality before the accident or in the next two weeks; then a lesion appeared on the upper lid and enlarged rapidly. The growth resembled a hematoma but changed within two months to a firm, unyielding mass. Partial resection of the tumor and radiation therapy were employed. The eye was removed two years after this operation. Biopsy specimens from the surrounding areas showed no residual tumor, and no evidence of metastasis has been found. The boy is in good health; he has developed normally and presents no defects other than the loss of one eye. At present, nearly seven years after the appearance of the initial lesion, there is no reason to suspect a recurrence of the malignant growth. Ralph W. Danielson.

Nuti, F. **An atypical case of Sturge-Weber's syndrome.** Boll. d'ocul. **27**:734-738, Nov., 1948.

A 20-day-old girl had a nevus flammeus, resembling a telangiectatic angioma, on the right cheek and eyelids, congestive glaucoma of the right eye and slight enlargement of the right cornea. Treatment with a 2-percent pilocarpine solution seemed satisfactory, but at the age of two years a typical excavation of the right disc was observed. The angioma gradually disappeared. K. W. Ascher.

Paufique, Offret, G., and Vouters. **Peripheral glioma of the orbit. A clinicopathologic study.** Arch. d'opht. **9**:9-26, 1949.

The authors deplore the confusion existing in the literature and in the current textbooks on orbital tumors, particularly the tumors of the optic nerve which are known as gliomas, neurinomas, or schwannomas. They point out the close relationship existing between the solitary nerve tumor and von Recklinghausen's disease. In the latter the diagnosis is facilitated by the associated lesions while in the isolated neurinoma diagnosis can only be made on the basis of microscopic examination. The relative frequency of isolated neurinoma of the optic nerve is stressed and its slow and usually benign evolution is described. Radiotherapy is of no value and the only treatment is surgical excision. This is always indicated because of the possibility of malignant changes and because of changes in the optic nerve resulting from pressure. The results of surgery are generally good; the exophthalmos disappears, usually leaving a slight degree of enophthalmos with slight limitation of motion. Visual acuity improves with disappearance of the papilledema. Phillips Thygeson.

Saebø, Johan. **Lipoma conjunctivae in three generations.** Acta ophth. **26**:447-450, 1948.

Lipoma of the conjunctiva at the outer angle of the right orbit is reported in

three generations. The inheritance is dominant and the tumor was larger in each succeeding generation. (2 figures, 1 table.) Ray K. Daily.

Suárez Villafranca, M. R. **Intraocular and orbital tumors.** Arch. Soc. oftal. hispano-am. **9**:67-90, Jan., 1949.

The diagnosis of eight intraocular and six orbital tumors is discussed. The slow evolution of sarcoma of the choroid in contradistinction to the rapid growth of sarcoma of the ciliary body is noteworthy, and the fundus picture of exudative retinitis in the case of intraocular cysticercus is worth remembering. (16 figures.) Ray K. Daily.

17

INJURIES

Atkinson, W. S. **Delayed keratitis due to mustard gas (dichlorodiethyl sulfide burns).** Arch. Ophth. **40**:291-301, Sept., 1948.

Late corneal lesions develop more frequently in cases with greater exposure to mustard gas and in those of greater susceptibility to it. The condition is aggravated if the eyes are bandaged during the acute stage that follows exposure to mustard gas. After recovery from acute symptoms, which in severe burns last from two to eight months, and sometimes longer, the patient is practically free from symptoms for eight years or more. Photophobia, lacrimation and failing vision mark the onset of the late corneal lesions. Superficial haze of the cornea just beneath the epithelium in the area of the palpebral fissure, lines or striae in the substantia propria and folds in Descemet's membrane may precede the formation of deposits of cholesterol and fat. These deposits increase in size, break through the epithelium and produce an exacerbation of the symptoms of irritation. Later, there is a heaping up of hard, degenerative tissue on the cornea. The scarred cornea is so irregular that vision is improved only with contact lenses. There are also pale, triangular patches on either side of the cornea in the area of the palpebral fissures that resemble lesions produced by surface application of beta radiation. Intracorneal hemorrhages occur and seem to arise from the large varicose vessels, which extend up to the limbus. Recognition of the late effects of mustard gas is important, so that claims of veterans of World War I may be justly handled. Ralph W. Danielson.

Knudtzon, Karsten. **The prognosis of scotoma helieclipticum. Follow-up of 47 patients injured in July 1945.** Acta ophth. **26**:469-494, 1948.

A review of the literature precedes the tabulated report of the ocular examination of 47 patients 18 months after injury by a solar eclipse. Forty had ocular damage. The damage produced by watching a solar eclipse without adequate protection is severe and permanent and justifies public warning before an eclipse. The usual inadequate sun glasses give a false sense of security. Knudtzon also warns against Bates' and Huxley's advice to accustom the eyes to direct sunlight. Ray K. Daily.

Lindblom, K. **Localization of foreign bodies in the eye by bone free radiography.** Acta ophth. **36**:439-440, 1948.

Lindblom describes his mofidication of the Vogt method of bone-free radiography for localization of foreign bodies in the anterior ocular segment. (4 figures.) Ray K. Daily.

Minton, Joseph. **Occupational diseases of the lens and retina.** Brit. M. J. pp. 392-394, March 5, 1949.

Protective care of the workers must be taken, the author states, or soon there will be reports of severe anemias and

cataracts in industries in which workers are exposed to molten glass or metal, ultraviolet radiation, high-tension electric currents and Xrays.

Theodore M. Shapira.

Saebø, Johan. **Automutilatia bulborum. A rare case of self-mutilation in an epileptic.** Acta ophth. **26**:451-453, 1948.

An epileptic, 25 years old, destroyed both of his eyeballs, apparently painlessly, under the illusion that this action would lead to a cure of his epilepsy and subsequent restoration of vision. He sectioned the upper lids and conjunctiva with the nail of the index finger, and then introduced the finger behind the eyeballs, and emptied them of their contents.

Ray K. Daily.

18

SYSTEMIC DISEASE AND PARASITES

Bucek, Alois. **Stevens Johnson syndrome.** Lekarske Listy **4**:203-204, May, 1949.

A case of Stevens-Johnson syndrome in a boy aged 2½ years is presented with two striking pictures.

F. H. Haessler.

Cass, E. **Reiter's disease.** Arch. Soc. oftal. hispano-am. **9**:176-179, Feb., 1949.

To the 200 cases of Reiter's disease reported in the literature the author adds one more case. The general examination was negative and therapy ineffective. The distinguishing feature was the rapid alleviation of some symptoms and the appearance of others, and the occurrence of interstitial keratitis, which is reported for the first time. Ray K. Daily.

Croom, J. H., and Scott, G. I. **Retinal and vascular damage in long-standing diabetes.** Lancet **1**:555-558, April 2, 1949.

The authors examined 60 patients who had diabetes from 15 to 26 years. Fifteen patients were free of any degenerative disease, they had neither retinopathy nor vascular changes, although one of them had had diabetes over 26 years. Only 18 patients presented typical diabetic retinopathy and 9 of them had normal retinal arteries, whereas the others had only slight arteriosclerotic or hypertensive changes. Some factor other than arteriosclerosis must be responsible for the retinopathy. The Kimmelstiel-Wilson syndrome or intercapillary glomerulosclerosis characterized by hypertension with edema of nephrotic type, massive albuminuria and renal or cardiac decompensation was present in two patients only.

R. Grunfeld.

Curtis, A. C., and Grekin, R. H. **Sarcoidosis: treatment with calciferol and dihydrotachysterol.** Tr. Am. Acad. Ophth. pp. 344-351, March-April, 1949.

Of 19 patients with sarcoidosis (4 had ocular lesions), 9 of whom were treated with calciferol and 5 with dihydrotachysterol, 3 were considered cured and 5 were improved. Both drugs increase the serum calcium and the excretion of serum phosphorus. Toxic reactions are not infrequent and occur less often if the calcium and nonprotein nitrogen is increased. It is not yet known which drug is more desirable. Both seem to produce approximately the same results. The toxic symptoms apparently occurred more slowly in patients treated with dihydrotachysterol. The optimal dose of calciferol is between 150,000 and 300,000 units daily; 3.75 mg. dihydrotachysterol is usually administered daily for three days and then reduced to 1.5 mg. The epithelioid cell reaction in sarcoidosis is apparently due to a phospholipid abnormality and the beneficial effect of calciferol and dihydrotachysterol is associated with the increased secretion of phosphorous. The authors believe that this treatment is not the ultimate one, but consider it more effective

than other treatments now in use.
Chas. A. Bahn.

Giardini, A. **Effect of methylthiouracil on the manifestations of Basedow's disease.** Boll. d'ocul. **27**:706-721, Nov., 1948.

Seventeen Basedow patients were treated with methylthiouracil and the gravity of their signs and symptoms was listed in tables which contained the exophthalmometer measurments, estimations of the lid edema, 12 eye signs of Graves, Stellwag, Dalrymple, Gräfe, et altera, pupillary changes, and the basal metabolism figures. About half of the patients showed a slight reduction of their exophthalmos. Patients with reduced dark adaptation did not respond to methylthiouracil unless high additional doses of vitamin A were administered. (2 tables, references.) K. W. Ascher.

Iribarren, R. **A case of subconjunctival filaria Loa loa.** Arch. de oft. de Buenos Aires **23**:302-308, Oct., 1948.

This nematode and accompanying symptoms are described at length. A case is described in which a cyst containing the filaria was removed from a conjunctival sac and other microfilaria were demonstrable in the blood-stream. (4 figures, references). Edward Saskin.

Scheie, H. G. **Ocular changes associated with scrub typhus.** Arch. Ophth. **40**:245-267, Sept., 1948.

The eyes of 451 patients with scrub typhus were studied weekly for evidence of disease. Conjunctival injection was present in 38 percent, and subconjunctival hemorrhages in 6.4 percent. Ecchymosis, eschar of the eyelid, fixation nystagmus were seen occasionally. There was engorgement of retinal veins in 67 percent, retinal edema in 36; retinal hemorrhages and retinal exudate, uveitis and vitreous opacities in a few patients. Pathologic studies of eyes obtained at autopsy revealed that a subacute diffuse choroiditis was the basic lesion. The fundus changes not seen in other febrile diseases in this area were frequently helpful in diagnosis. The lesions in the eye are a fair index of convalescence.
Ralph W. Danielson.

Woods, A. C. **Sarcoidosis: the systemic and ocular manifestations.** Tr. Am. Acad. Ophth. pp. 333-343, March-April, 1949.

After a historical review, a brief résumé of the extraocular symptoms is given. Among these are increased sedimentation rate, increased globulin fraction and anergy to as much as 10 mg. tuberculin. Negroes are more susceptible in the ratio of 6 to 1. The ocular lesions are chronic granulomatous processes with epithelioid cell nodules. Although the individual lesions may be benign, secondary glaucoma and ocular atrophy are not infrequent. The eyes were involved in 44 of 94 cases of sarcoidosis. The eyes are frequently involved early in the disease, which may be associated with uveo-parotid fever and Mikulicz syndrome. Some authors consider that 5 to 10 percent of uveitis is due to sarcoidosis. Almost all parts of the eye may be involved. Nodular uveal lesions with interlacing vascular patterns and large gray precipitates are frequent. Primary choroidal and retinal lesions are rare. Chas. A. Bahn.

19

CONGENITAL DEFORMITIES, HEREDITY

Albertto, Benjamin. **Marfan's syndrome.** Arch. de oft. de Buenos Aires **23**: 240-252, Sept., 1948.

A case of Marfan's syndrome in a girl, 12 years of age, is presented in great detail. A. G. Wilde.

Bernoulli, R. **The mechanism of persistence of the hyaloid artery.** Ophthalmologica **117**:169-179, March, 1949.

A rare congenital anomaly in a seven-year-old boy is described. The right eye was highly myopic but seemed to have adequate vision. The left eye was slightly microphthalmic. A heavy vessel-bearing strand of gray tissue originated in the region of the disc, traversed the vitreous cavity forward, downward and laterad and was inserted on the posterior surface of the lens a little below the posterior pole. No blood vessels could be made out in the retina which appeared to occupy a normal position. The strand in the vitreous is interpreted as a persistent hyaloid artery with hypertrophic glial sheaths. This overdevelopment of the glial sheaths probably prevented the development of the retinal vessels. Peter C. Kronfeld

Broendstrup, J. M. **Posterior embryontoxon in three generations. Anomaly of development of the anterior chamber of the eye with annular opacity of the cornea and membrane before the chamber angle.** Acta ophth. **26**:495-507, 1948.

The literature is reviewed and a family with embryontoxon reported. The bilateral malformation consisted of a massive adhesion between the iris and cornea. Around the entire circumference there was a whitish gray homogeneous peripheral band-like thickening on the posterior surface of the cornea, 0.5 to 2 mm. wide with a sharp serrated pupillary edge, and a peripheral boundary that faded gradually into clear cornea. There was definite hypoplasia of the iris and its stroma seemed to fuse with the corneal band. At 35 years of age glaucoma was discovered in one eye. Seven cases of this anomaly occurred in three generations of the family. All affected members were fair, short, blue eyed, and had high cheek bones. The unaffected members were dark and tall. (5 figures.) Ray K. Daily.

Esteban, A., and Wolf, J. A. **Bilateral aniridia with ptosis and embryontoxon.** Arch. de oft. de Buenos Aires **23**:141-148, July-Aug., 1948.

A twenty-eight-year old woman who had one son with aniridia and another with congenital heart defect had bilateral ptosis with enophthalmos, congenital bilateral aniridia and nystagmus. The marked photophobia was mitigated somewhat by her ptosis. She had no strabismus, and convergence was normal. The cornea showed a peripheral clouding 2 to 4 mm. wide in the superficial layers resembling an arcus senilis, but more irregular in outline. There was anterior and posterior cataract. The visual acuity was limited to counting fingers at two meters.

A. G. Wilde.

Hallermann, W. **"Bird-face" due to deformation of the mandible and congenital cataract.** Klin. Monatsbl. f. Augenh. **113**: 315-318, 1948.

Two cases of congenital malformation of the mandible with considerable shortening of its body which leads to the appearance of "bird face" are reported. Both patients had had bilateral congenital cataracts in each eye. It is not known whether the two abnormalities are related. (4 figures.) Max Hirschfelder.

Lowe, R. F. **The eyes in mongolism.** Brit. J. Ophth. **33**:131-175, March, 1949.

Mongoloid facies and almond shaped palpebral apertures do not invariably occur in the syndrome mongolism. One of the most important signs is the general retardation of growth affecting all the tissues of the body even to the extent of retention of fetal characteristics throughout life. In 67 patients, of which 40 were over 25 years of age, the skulls and all the skull bones examined exhibited a marked retarding of growth. Four skulls even had persistent frontal sutures. The diameters of the orbits were small and the inclination of the axis was 75 degrees

instead of the normal 45. This brings about a palpebral aperture which is more oblique and shorter than the normal. Epicanthus is normal in babies and disappears in the first few years. In mongolism it remains a little longer and is almost always gone by the 12th year. The lids and lacrimal systems are usually normal. The iris presents two characteristic changes: a general poverty of stromal fibers and noticeable depigmentation. Speckling of the iris is common. Arcuate lens opacities, the most common, develop during fetal life owing to the presence of abnormal capsulo-pupillary vessels, sutural opacities occur in the anterior Y sutures of the fetal nucleus and flake opacities are found in the juvenile and adult nuclei. About one third of subjects had very high myopia. Nystagmus was found in nine and in only 2 was it of cerebral origin. It is not considered characteristic of mongolism. Strabismus occurs about 20 times as often as in the general population. (23 figures.)

Morris Kaplan.

Lutman, F. C., and Neel, J. V. **Inheritance of arachnodactyly, ectopia lentis and other congenital anomalies (Marfan's syndrome) in the E family.** Arch. Ophth. **41**:276-305, March, 1949.

Marfan's disease is a syndrome which in its fullest expression is characterized by an elongate, slender body build, especially evident in the extremities, skeletal deformities (kyphosis, scoliosis, pigeon breast, pes planus, hammer toes), dolichocephalic skull, poorly developed and hypotonic musculature, laxity of the joints and ligaments, scanty subcutaneous fat, malformation of the ears, malformations of the lungs, congenital heart disease, and ocular anomalies, especially ectopia lentis. There is great variability in the degree to which these traits are manifest.

The clinical records of several hundred visits by members of the E family have been accumulating at the Strong Memorial and Rochester Municipal Hospitals since 1928. In 1941, an attempt was made to reëxamine all the members who had hospital records. In a kinship of 40 persons, 17 members probably had Marfan's syndrone (arachnodactyly, ectopic lentis, indications of cardiac abnormalities and other congenital defects). There was a great variability in the expression of the syndrome in the affected members of the kinship. In addition to classic cases, there existed in this one family members so mildly affected that the diagnosis would be unsuspected or in doubt were it not for their genetic background. Ocular anomalies observed in all persons studied were, in addition to ectopia lentis or coloboma of the lens, abnormal zonular fibers, an iris lacking in the usual surface trabeculae and crypts, deficiencies of uveal pigment, particularly at the periphery of the iris, and amblyopia. In several cases there were other ocular defects. The syndrome is inherited as though due to one or more dominant autosomal genes. Although a final decision is not possible, the bulk of the evidence suggests that the entire syndrome may be due to one gene only whose expression is greatly influenced by other genetic, and possibly by environmental, factors.

Ralph W. Danielson.

Straith, C. L., and Lewis, J. R. **Associated congenital defects of the ears, eyelids and malar bones (Treacher Collins syndrome).** Plast. and Reconstruct. Surg. **4**: 204-213, March, 1949.

In addition to a review of the literature, which is scanty, four cases of Treacher Collins syndrome are reported. The characteristics are as follows: flattened malar eminence, deficient lower orbital margin, oblique palpebral fissures,

bilateral notches in the outer third of the lower eyelids, eyelashes absent on medial two-thirds of lower eyelids, receding chin, and high, narrow, prominent front teeth, bilaterally deformed external ears, with frequently associated abnormalities of the external auditory meatus and loss of hearing. Plans for the plastic repair of these defects are discussed. Alston Callahan.

20

HYGIENE, SOCIOLOGY, EDUCATION, AND HISTORY

Eames, T. H. **The effect of glasses for the correction of hypermetropia and myopia on the speed of visual perception of objects and words.** J. Educational Research **42**:534-540, March, 1949.

In 100 children an increase in speed of work perception followed the use of glasses for correction of refractive errors. The correction of lower degrees of hypermetropia than of myopia tends to produce increment in a larger percentage of cases per dioptric level. F. H. Haessler.

Jokl, A. **Death from eye disease and occurrences of death in ophthalmological practice.** Ophthalmologica **117**:129-146, March, 1949.

The author reviews the eye diseases which have caused the patient's death, either directly or through circumstances which were the direct sequel of the eye disease or intimately connected with it. The diseases are grouped under the following headings: hemorrhages from the conjunctiva in hemophilia and from vascular tumors and bacterial diseases that gained entrance to the body through the conjunctiva or the lids, perforating injuries, or orbital cellulitis. The severe systemic intoxication due to the local application of "lash lure" is mentioned. Well known examples of death after operations are the fatal outcome of dacryocystectomies in chronic suppurative dacryocystitis and of enucleations in panophthalmitis. The malignant primary tumors of the eye and its adnexa are discussed in detail. Fear of blindness or unrelieved neuralgic pain may drive a patient to suicide. The first pair of bifocals makes the patient more liable to meet with an accident. Peter C. Kronfeld.

Mercier, Armand. **Visual aptitudes in railroad and aviation employees.** Ann. d'ocul. **182**:24-31, Jan., 1949.

The relative merits of the requirements are discussed. The author believes that railroad employees require better sight than aviators. Chas. A. Bahn.

Sachs, M. **Nearly one hundred years of the ophthalmoscope.** Arch. Ophth. **40**: 268-272, Sept., 1948.

This paper gives interesting facts about von Helmholtz and describes incidents in the discovery of the ophthalmoscope. Ralph W. Danielson.

NEWS ITEMS

Edited by DONALD J. LYLE, M.D.
601 Union Trust Building, Cincinnati 2

News items should reach the editor by the 12th of the month but, to receive adequate publicity, notices of postgraduate courses, meetings, and so forth should be received by the editor at least three months before the date of occurrence.

DEATHS

Dr. Harry Monroe Hendershott, Portland, Oregon, died March 26, 1949, aged 69 years.

ANNOUNCEMENTS

EGYPTIAN MEDAL FOR SCIENTIFIC WORK

To encourage scientific ophthalmic work, the Ophthalmological Society of Egypt will award each year a gold medal for the most valuable contribution of the year.

The competition is open to all members of the society of less than 20 years' practice, whether living in Egypt or outside of the country. Candidates desiring to enter the prize competition should submit their theses, in three typed copies, not later than the first of December each year.

In making the award, the committee will consider: (1) The originality of the work in its conception and execution; (2) its application to the major problems of ophthalmology; and, (3) general presentation.

Further information may be obtained by addressing: Dar El Hekma, 42 Kasr El Ainy Street, Cairo, Egypt.

CALIFORNIA POSTGRADUATE COURSE

The University of California Medical School, San Francisco, is offering a postgraduate course in ophthalmology from September 12th through September 17th. The course is open only to graduates of medical schools approved by the Council on Medical Education and Hospitals of the A.M.A. The fee for the course is $60.00, payable at the time of enrollment.

Dr. Frederick C. Cordes, clinical professor of ophthalmology, University of California Medical School, is general chairman of the course. Officers of instruction will be: Dr. Samuel D. Aiken, Dr. Crowell Beard, Dr. Dudley P. Bell, Dr. George S. Campion, Dr. Joseph W. Crawford, Dr. C. Allen Dickey, Dr. Owen C. Dickson, Dr. David O. Harrington, Dr. Margaret Henry, Dr. Michael J. Hogan, Dr. Bertram V. A. Low-Beer, Dr. Robert N. Shaffer, Dr. Joseph G. Smith, and Dr. Phillips Thygeson.

Further information may be obtained by addressing: Dr. Stacy R. Mettier, head of postgraduate instruction, medical extension, University of California Medical Center, San Francisco 22, California.

Preceding the postgraduate course in ophthalmology will be a course in otorhinolaryngology, September 5th through 9th.

TORONTO OFFERS GRADUATE TRAINING

The University of Toronto, Faculty of Medicine, offers a postgraduate course in ophthalmology extending over three years. The graduate instruction in ophthalmology in the teaching hospitals in Toronto has been coördinated under the direction of the university. The first year on a fellowship, the value of which is approximately $1,400, the student spends in one of the basic sciences of ophthalmology, and the final two years are spent on the intern service of one or more of the university teaching hospitals. Approximately four hours of didactic teaching are arranged for the students by members of the staff each week from October to May. On Saturday morning, staff ward rounds are made at the Toronto General Hospital and are attended by the interns from the other teaching hospitals.

A sound knowledge of neurology and metabolic diseases is desirable. The following courses are given: geometric and physiological optics, physiology of the eye, principles and practice of biomicroscopy, perimetry, ocular therapeutics, medical ophthalmology, pathology of the eye, bacteriology and external diseases of the eye, embryology and developmental anomalies of the eye, ocular motor anomalies, anatomy of the orbit, skull, and brain, radiological ophthalmology, industrial ophthalmology, intraocular and plastic surgery, pathology of the visual pathways, refraction, neuro-ophthalmology, glaucoma. Senior interns are given instruction in the preparation and presentation of scientific papers.

The fee for instruction is $50.00 per year payable to the chief accountant, University of Toronto. An application for appointment may be made to the professor of ophthalmology, Faculty of Medicine, University of Toronto. Appointments are made in December to commence on the following July 1st.

ORTHOPTIC TRAINING COURSE

The Rochester (New York) Orthoptic Center is receiving applications for its next training course for orthoptic technicians. The course is accredited by the American Orthoptic Council. Information may be obtained from the Rochester Orthoptic Center, 208 North Goodman Street, Rochester 7, New York.

MISCELLANEOUS

LIONS CLUB SCHOLARSHIPS

On June 21st, the Lions Club of New York presented four $500 scholarships to graduate students of New York University College of Medicine who

are planning to become eye specialists. The presentation took place at the annual Ladies' Day luncheon at the Savoy Plaza.

Walter Hoving, president of the Hoving Corporation, in behalf of the Lions Club, handed a $2,000 check to Dr. Daniel B. Kirby, professor of ophthalmology, New York University College of Medicine. Dr. Kirby said the funds would enable four students to undertake research projects, adding that even such small sums of money might be instrumental in obtaining important results.

The four students who will receive the scholarships are Dr. Irwin Cohen, Dr. Thomas Heslin, Dr. James Mayer, and Dr. Arthur Smith.

Ernest R. Fryxell, chairman of the Lions Club Blind Aid and Eye Conservation Committee, announced that the organization would suggest to the 7,203 Lions Clubs throughout the country that they undertake similar scholarships for ophthalmologists.

Earlier recipients of the Lions Club of New York scholarships are: Dr. Edward P. Danforth, Dr. Charles Goldsmith, Dr. Jonathan L. Harris, and Dr. Hugh McGee for the year, 1946; Dr. Edward Buckley, Dr. George R. Kolodny, Dr. Nathaniel Robinson, and Dr. Horace Shreck, for 1947; Dr. Goodwin Breinin, Dr. Edwin Kent, Dr. Walter Mayer, and Dr. Charles Toomey, for 1948.

Better Vision Institute

New members present at the annual meeting of the Better Vision Institute, June 10th, at the Park Lane Hotel, New York, were John Wiseman of Wiseman Optical Company, London, England; Tom Hood and Fred Soden of Continental Optical Company; Dr. John J. Brown of Perth Amboy, New Jersey; and Ray Farnum of Bausch & Lomb Optical Company.

Elections were held of new directors to serve two-year terms, and new finance committee members to serve for one year.

Carolinas meeting

On September 12th through 15th, at the Hotel Poinsett, Greenville, South Carolina, the North Carolina Eye, Ear, Nose, and Throat Society and the South Carolina Society of Ophthalmology and Otolaryngology will hold a joint meeting. The following program will be heard:

Dr. A. D. Ruedemann, professor of ophthalmology, Wayne University, Detroit, Michigan: "The differential diagnosis between unilateral and bilateral ocular protrusion"; "The end results with new radium-D applicator in comparison to radon"; "Ocular manifestations of allergy."

Dr. Peter C. Kronfeld, Department of Ophthalmology, Illinois Eye and Ear Infirmary, University of Illinois, Chicago: "Differential diagnosis of acute glaucomas"; "Prognosis of retinal detachment"; "Newer drugs in ophthalmology."

Dr. Rudolph Aebli, professor of ophthalmology, New York University, Bellevue Medical Center, Post-Graduate Medical School, New York: "The relationship of muscle imbalances to the palpebral aperture and pseudoptosis"; "Principles of ocular muscle surgery"; "Congenital muscle anomalies."

Dr. Carl C. Johnson, associate, Department of Ophthalmology, Harvard University, Boston: "Surgical treatment of ptosis"; "The diagnosis and surgical treatment of glaucoma."

Dr. Preston C. Iverson, New York: "Neoplasms of the lip, nose, and eyelid and plastic repair of the lesions"; "Congenital deformities of the face."

Dr. Louis H. Clerf, Philadelphia: "Cough viewed from otolaryngologic standpoint"; "Paralysis of larynx: Surgical treatment"; "Malignant neoplasms of larynx."

Dr. Kenneth M. Day, Pittsburgh: "Clinical management of deafness"; "Meniere's disease."

Dr. Russell A. Sage, Indianapolis: "Diseases of the mouth and tongue."

Officers of the South Carolina Society of Ophthalmology and Otolaryngology are: President, Dr. Pierre G. Jenkins; vice-president, Dr. Murdock Walker; secretary-treasurer, Dr. Roderick Macdonald.

Officers of the North Carolina Eye, Ear, Nose, and Throat Society are: President, Dr. James Harrill; vice-president, Dr. G. M. Billings, secretary-treasurer, Dr. MacLean B. Leath.

West Virginia officers

The officers of the West Virginia Academy of Ophthalmology and Otolaryngology are: President, Dr. Garnett P. Morison, Charles Town; 1st vice-president, Dr. Charles T. St. Clair, Jr., Bluefield; 2nd vice-president, Dr. Arthur C. Chandler, Charleston; treasurer, Dr. Frederick C. Reel, Charleston; secretary, Dr. Melvin W. McGehee, Huntington; directors, Dr. Eugene C. Hartman, Parkersburg, and Dr. Ivan Fawcett, Wheeling.

Personals

To give fourth Proctor Lecture

On Friday evening, September 16th, Dr. Jonas S. Friedenwald, Baltimore, will deliver the fourth annual Francis I. Proctor Lecture on Ophthalmology at the University of California Medical School, San Francisco. The subject of Dr. Friedenwald's address will be "Further studies on diabetic retinopathy."

Research on corneal transplants

Dr. A. E. Maumenee, head of the Department of Ophthalmology, Stanford University School of Medicine, San Francisco, will do research work on corneal transplants under a contract with the National Advisory Council of the U. S. Public Health Service.

In announcing the receipt of the grant, Dean Loren R. Chandler of the medical school said that the funds include an allowance for a research fellow and that applications for the fellowship are requested by the medical school. The research grant is for one year but is subject to renewal.

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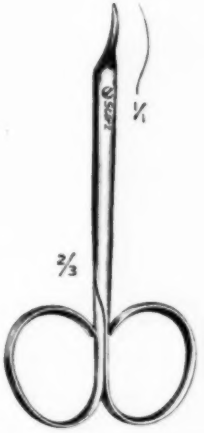

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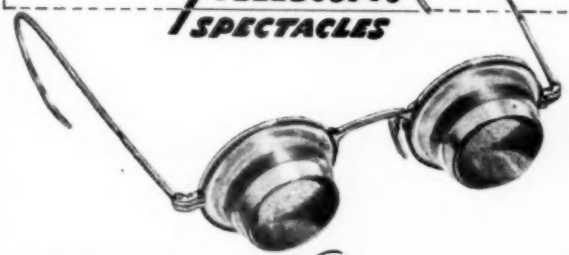

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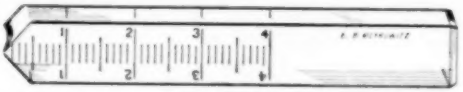

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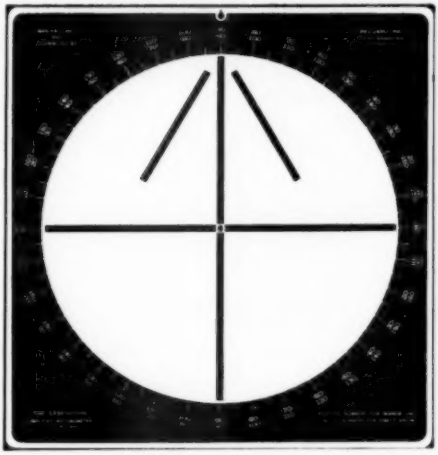

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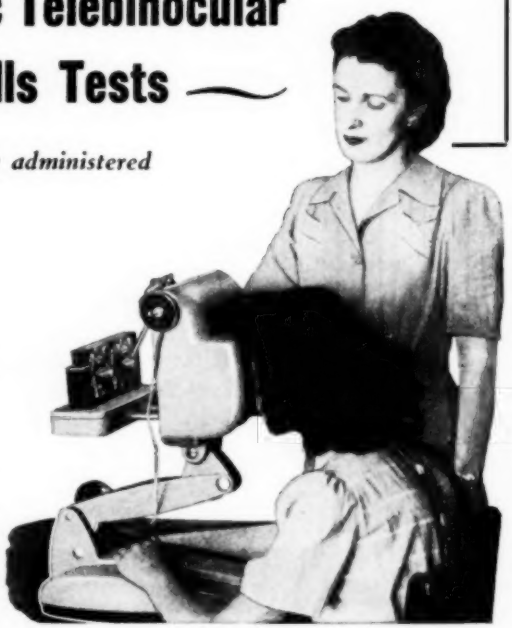

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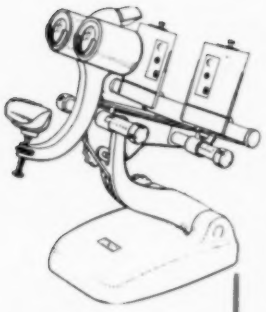

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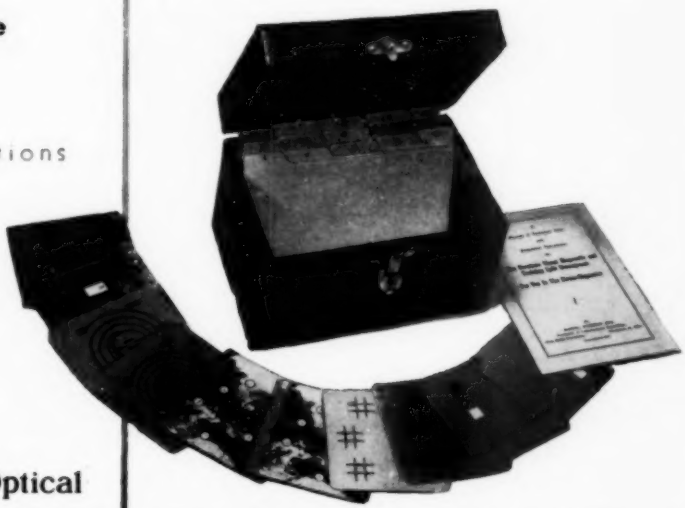

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